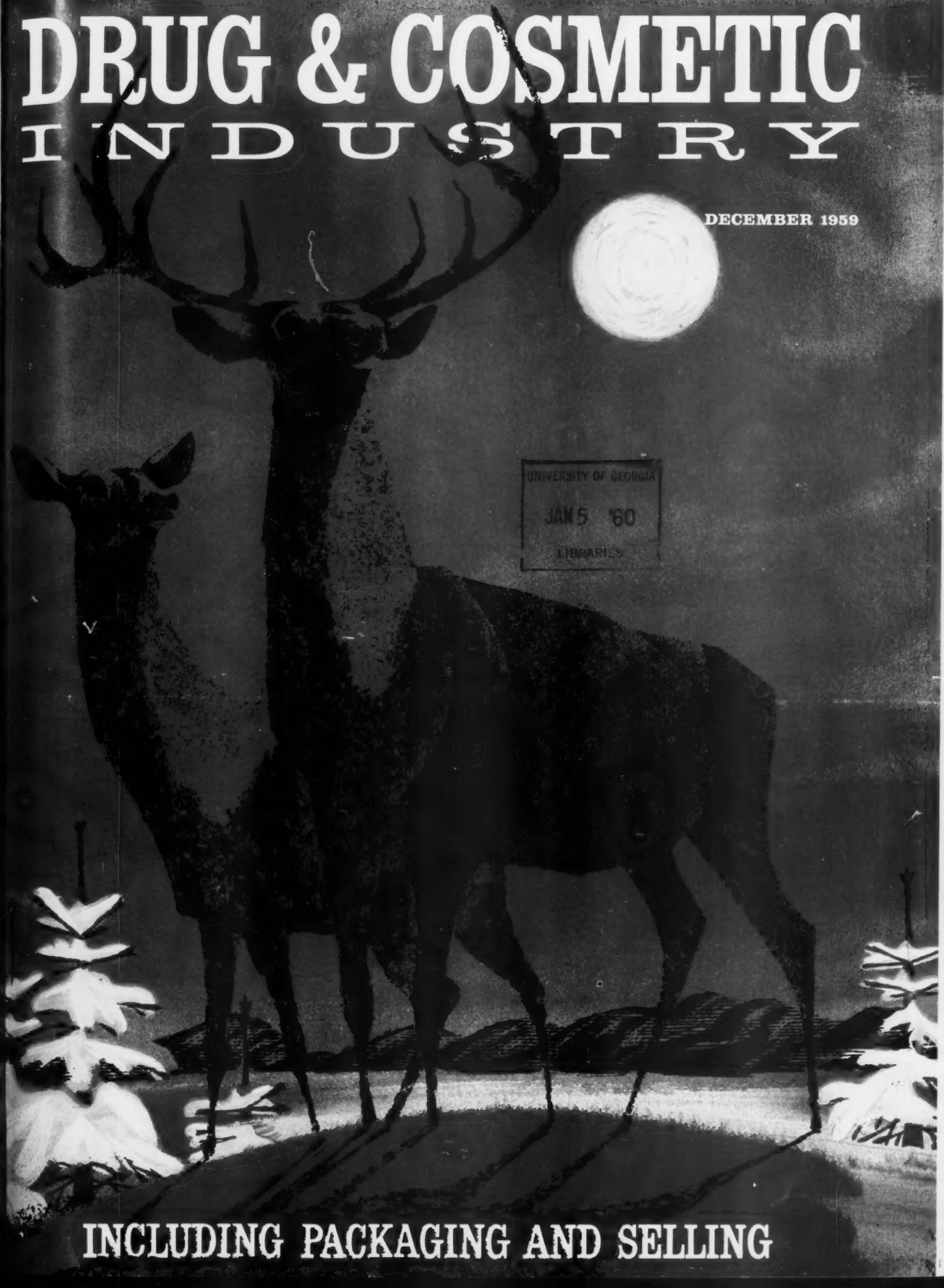
DRUG & COSMETIC INDUSTRY

DECEMBER 1959



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Drug and Cosmetic Industry

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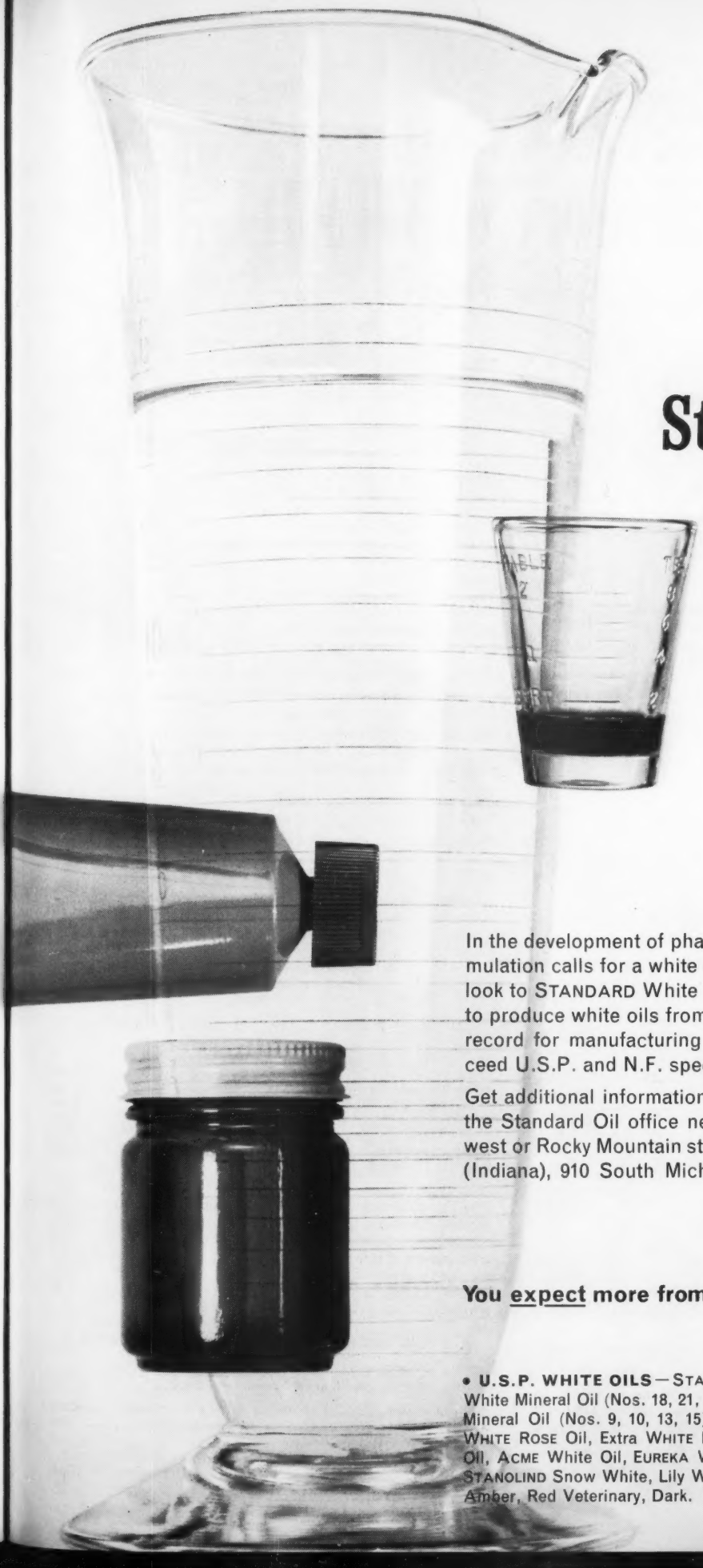

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INSIDE SCIENCE

New Expanded Edition

The Vital Story of VITAMIN A

by Science Writer

THE "FIRST" VITAMIN

Vitamin A was probably the first to be discovered. As early as 1909 Hopkins and Stepp found that certain fat-soluble substances were necessary for the growth of mice and rats. Between 1913 and 1915, working independently, the teams of McCollum and Davis, and Osborne and Mendel revealed the existence of a fat-soluble fraction in butter, egg yolk and cod-liver oil, which was essential for the growth of laboratory animals. McCollum and Davis concluded that the unknown substance was organic in nature. They had, in effect, discovered vitamin A, even though they did not so name it.

An interesting point: McCollum and Davis noted that the word "vitamine," coined by Casimir Funk a year or so previously, might be used to describe the growth factor they had found. Subsequently, McCollum (and Kennedy) reversed this opinion and suggested that the unknown substances which induced growth be called *fat-soluble A* and *water-soluble B*. In their opinion these phrases better described the unknown factor. Casimir Funk disagreed, however, pointing out that, to be truly descriptive, the phrases should read *growth-promoting fat-soluble A*, etc. This obviously being cumbersome, Funk suggested the designations: vitamine A, vitamine B, and so on. These (with the final "e" omitted) are now firmly embedded in the language.

Other investigators worked on the problem of carotene, beginning in 1831 when Wackenroder isolated that substance from carrots. We shall see later how vitamin A and the carotenes, particularly beta carotene, are interrelated.

TRACKED DOWN

Various tries at isolating vitamin A were made in the 1920s. Investigators in Japan and England attempted without success to extract the elusive vitamin from cod-liver oil.

After establishing the structural formula of beta carotene, Paul Karrer of Switzerland turned his attention to vitamin A. He and his colleagues, using halibut-liver oil (which has a much higher potency than cod-liver oil) succeeded in determining the structure of the vitamin A molecule in 1931.

WHAT IT IS

Pure vitamin A crystals are pale yellow in color. They are soluble in fat and in fat solvents but not in water. The chemist's formula is $C_{20}H_{30}O$, expressing the vitamin's composition of carbon, hydrogen, and oxygen. Beta carotene has the formula $C_{40}H_{56}$.

Vitamin A is stable to light and heat, but is destroyed by oxidation and ultraviolet light.

Two vitamins A have been discovered. Vitamin A_1 occurs in animal products such as egg yolk, liver, butter, and in the livers of salt water fish. Vitamin A_2 is found in fresh-water fish livers.

As now used by pharmaceutical and food manufacturers, vitamin A is in liquid form — in solution in edible, vegetable oil — or in dry granular form in which tiny droplets of the liquid vitamin are encased in a dry, edible material.

ACTION

Human beings receive their vitamin A from many sources. They eat vegetable foods rich in beta carotene (a provitamin A) which is then converted by the body into a vitamin. They eat animal products which contain the vitamin. They eat processed foods which are fortified with beta carotene or vitamin A or both. They use pharmaceutical preparations of the vitamin, with or without other vitamins, for therapeutic or protective effect.

The liver has been found to be the main storage site of vitamin A. It is also lodged in the kidneys, lungs, adrenal glands, and body fat.

It is believed that provitamins A are converted to the vitamin in the intestinal wall, the liver, and other parts of the body through the action of the enzyme called carotenase.

Vitamin A is absorbed primarily in the healthy intestine and is carried in the lymph and blood to the body's storage depots.

HOW MUCH DO WE NEED?

According to the Food and Nutrition Board of the National Academy of Science — National Research Council, in its 1958 publication #589, vitamin A is needed daily (in various amounts depending on age and sex) to maintain good nutrition of healthy persons in the U. S. A. The following table expresses the Board's recommendations in International Units of the vitamin.

NATIONAL RESEARCH COUNCIL RECOMMENDATIONS FOR DAILY VITAMIN A INTAKE

Men (all ages)	5,000	Children (1–3 years)	2,000
Women (all ages)	5,000	Children (4–6 years)	2,500
Women (pregnant, second half)	6,000	Children (7–9 years)	3,500
Women (lactating)	8,000	Children (10–12 years)	4,500
Infants (2–6 months)	1,500	Boys (13–19 years)	5,000
Infants (7–12 months)	1,500	Girls (13–19 years)	5,000

The Food & Drug Administration of the U. S. Department of Health, Education and Welfare has set the following standards as being the *minimum* daily requirement. In other words, these amounts are the *least* which can be ingested to prevent recognizable signs of deficiency disease from developing. There is an opinion among nutrition experts that the *minimum* amount of a vitamin is not necessarily the best criterion.

F. & D. A. *MINIMUM* DAILY REQUIREMENTS OF VITAMIN A

(Measurements in U. S. Pharmacopeia (U.S.P.) units which equal International Units)

Men and Women	4,000	Children (1–11 years)	3,000
Adolescents (12–19 years)	4,000	Infants (to 1 year)	1,500

DEFICIENCIES AND MEDICAL USES

Correcting a vitamin A deficiency has little of the instant, dramatic impact that, for example, vitamin C has in curing scurvy.

Because of the body's ability to store quantities of vitamin A which are released as needed, a considerable time passes before the vitamin A deficiency develops.

Lack of enough vitamin A shows itself in several ways.

"Dark adaptation" of the eyes is diminished. Go from a brightly lighted place to one which is dim or dark; notice how your eyes need a few moments to adjust. This is known as *dark adaptation*. With vitamin A deficiency, the power of the eyes to make the adjustment quickly and completely is lessened, sometimes severely or dangerously.

The skin, too, becomes dry from lack of vitamin A. The linings of the hair follicles harden and become plugged, thus interfering with the secretion of the skin's oil glands.

Other epithelial tissues, such as the linings of the upper parts of the respiratory passages, the genito-urinary tract, the alimentary canal, may not function properly.

Vitamin A is necessary for growth. When children fail to gain weight a deficiency of the vitamin may be suspected.

Physicians treat the deficiency states with therapeutic doses of the vitamin. To prevent their development or recurrence they may prescribe supplementary dosages.

MICROGRAMS, U. S. P. UNITS, INTERNATIONAL UNITS

The measurement of vitamin A is made in *International Units* which may be abbreviated as I.U. or i.u.

One International Unit of vitamin A is equivalent to:

— 0.344 microgram of crystalline vitamin A acetate.
— 0.300 microgram of crystalline vitamin A alcohol.
— the activity of 0.6 microgram of pure beta carotene.
— one U. S. P. unit of vitamin A.

In everyday measurement, one ounce equals 94,500,000 International Units of vitamin A alcohol.

Vitamin A is available to pharmaceutical and food manufacturers in forms having standardized potencies as, for example, liquid products containing 1,000,000 units per gram or dry beadlets having 250,000 or 500,000 units per gram.

MEASURING VITAMIN A

The best known and most commonly used method of measuring vitamin A is the Carr-Price spectrometric assay. In this chemical test a measurable blue color appears when a reagent (antimony trichloride) is added to the vitamin. The so-called "blue value" when measured photometrically can be converted by a mathematical formula into International Units of vitamin A.

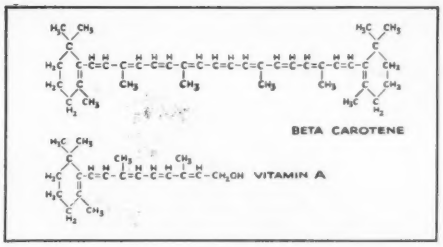
PROVITAMIN AND VITAMIN

The carotenes and vitamin A are known to be closely related. The former are known as precursors, or *provitamins*. It is one of nature's singular facts that the carotenes contain no vitamin A and yet have important vitamin A value. The body has a mechanism by which carotene is converted to vitamin A.

Four carotenoids: alpha-, beta-, and gamma carotene, and cryptoxanthin are known to be provitamins A. Of these, beta carotene is the most valuable in supplying the vitamin's value. The carotenes exist as colors in vegetable material. Example: carrots from which the word "carotene" was derived.

The chemical formulae of the carotenes show their relationship to vitamin A. This is demonstrated in the diagram that follows showing vitamin A and beta carotene.

Theoretically, one molecule of beta carotene could be expected to yield two of vitamin A. Actually this efficiency of conversion is not normally achieved in the human body.



GOOD SOURCES

Margarine, which has been fortified with vitamin A or with a combination of the vitamin and beta carotene (for safe coloring, plus nutritional value) supplies important amounts in our daily diet. Butter, too, can be a valuable source. It contains vitamin A in quantities which vary as the dairy cows' diet varies between seasons. Another good source of vitamin A is beef or calves' liver.

There are many foods which contribute vitamin A value through their supplies of the carotenes. Among these are apricots, beet greens, broccoli, carrots, kale, spinach, sweet potatoes, and turnip greens.

MOSTLY, IT'S MADE

After the chemical composition was determined by Paul Karrer and the product was crystallized by Holmes and Corbett, many attempts were made to synthesize the vitamin. The most successful, that of the Roche research team headed by Otto Isler, supplies a large portion of the world's requirements.

Vitamin A is also extracted from natural sources such as the liver of fish. Esthetically and practically, however, synthetic vitamin A has been found the most satisfactory for products used by human beings.

The U. S. production of synthetic (man-made) vitamin A is measured in tons. This huge annual production is enough to supply daily 170,000,000 people, the total population of the United States, with the 5000 international units (recommended by the National Research Council for daily adult intake) and still have enough synthetic vitamin A left over for use in animal feeds, pet foods, for export, etc. Of course, not everyone does receive his daily requirements through the medium of manufactured vitamin A. Yet, the *potential* is always there.

Pure beta carotene, so closely allied with vitamin A, also is man-made in large amounts for use in safely coloring and fortifying foods. Since it was first synthesized in Roche research laboratories, beta carotene Roche has been produced in ever-increasing quantities to meet the demands of the food industry for safe, sure, economical, yellow color with nutritional value as a bonus.

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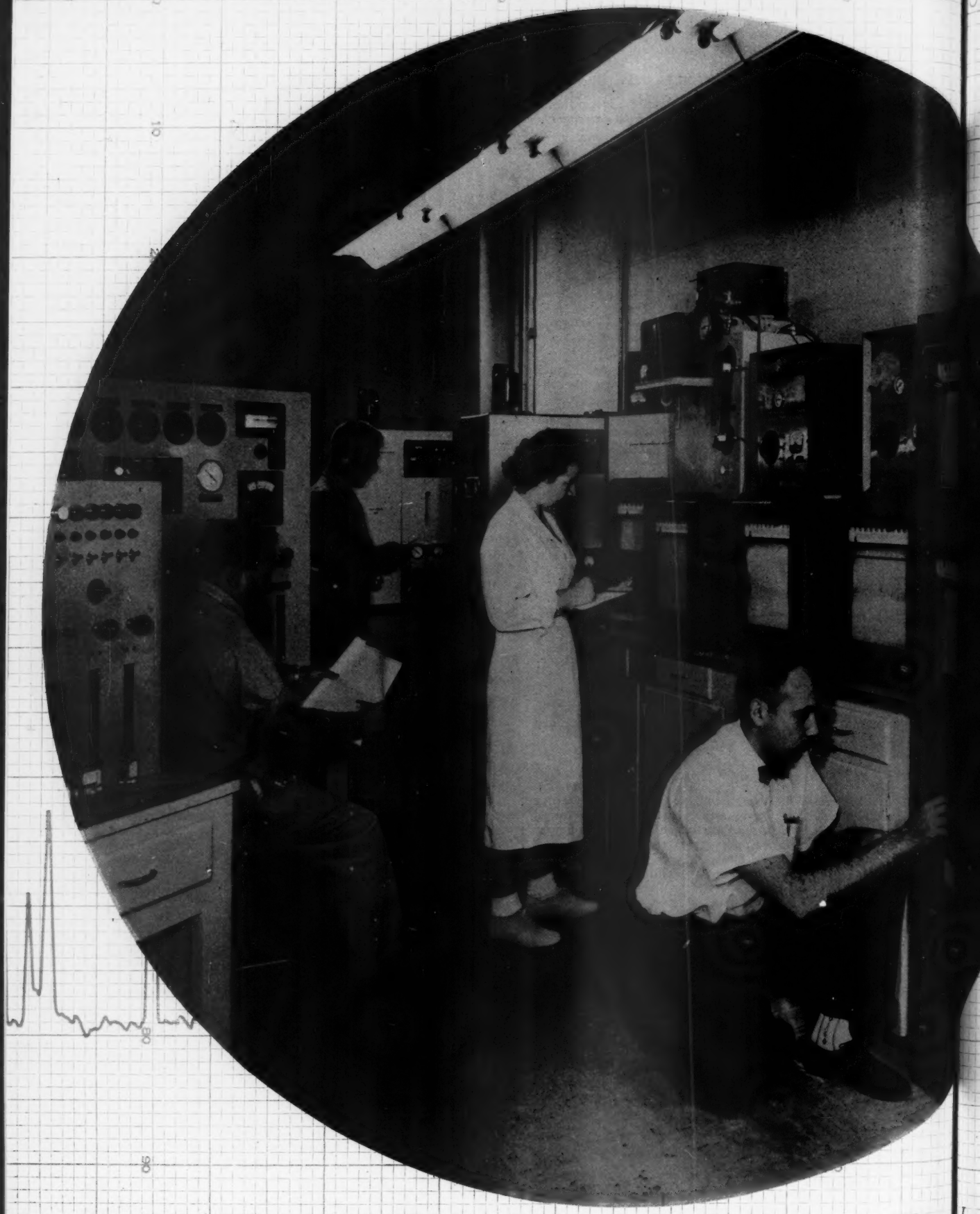
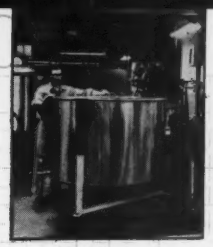
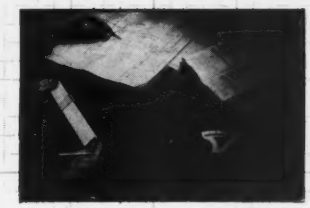
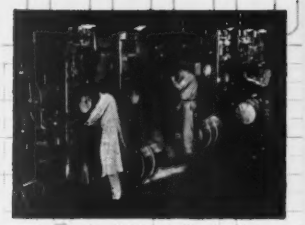




Perfume
Oil Production

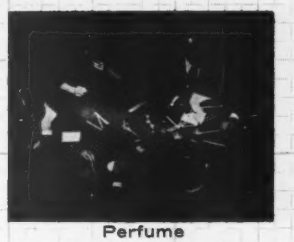


Chemical Engineering



Chemical Manufacturing

Quality Control



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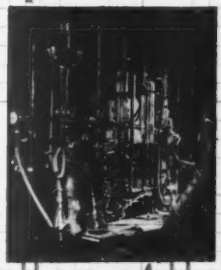

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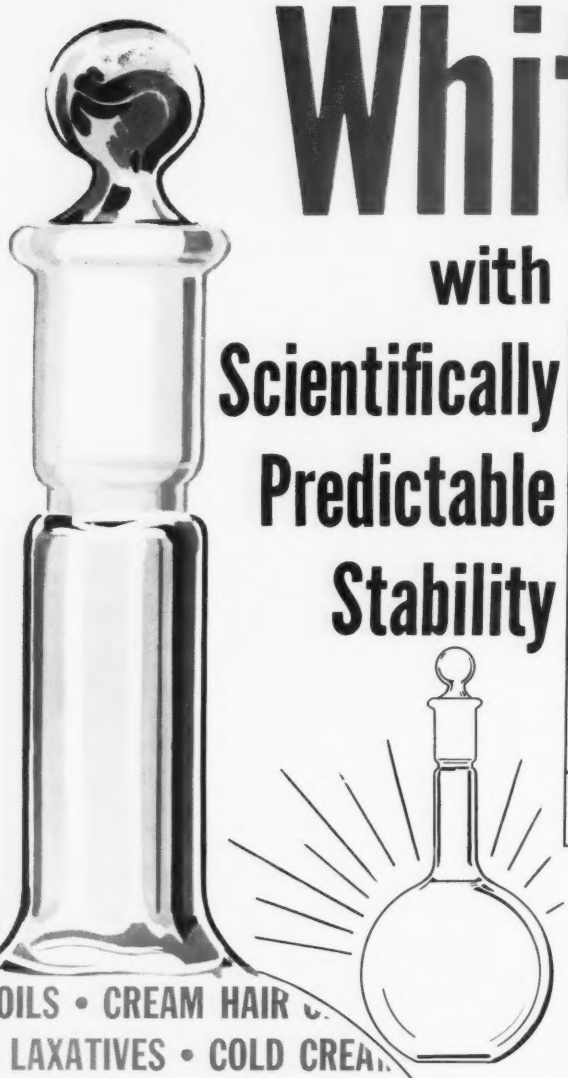

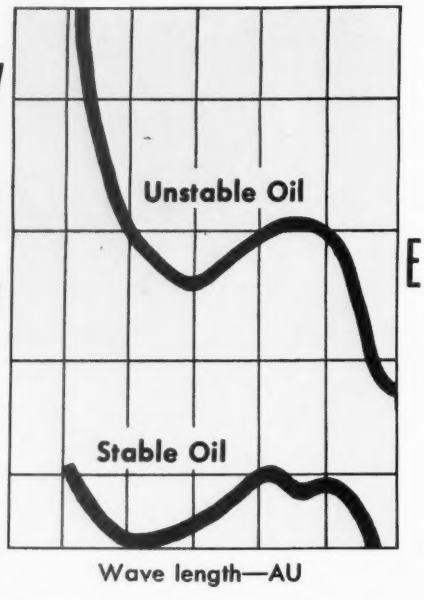

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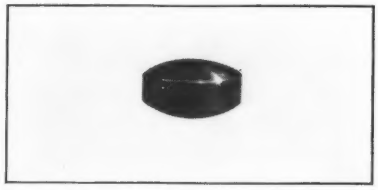
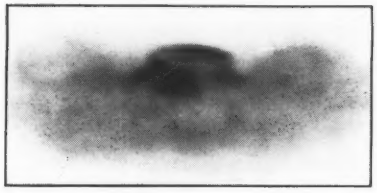


It's an enteric coating



and it works

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You may wish to check certain items in this advertisement and forward to those concerned in your company.

ROUTE TO:

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VERSATILE EMULSIFIER EASES FORMULATION, UPS PRODUCT SALABILITY

When formulation of soap-based cosmetic products is the order of the day, Dow triethanolamine is the key to easy, effective emulsification of new and different ingredients. It offers a clear-cut economic advantage, often doing the work which formerly required two or three different agents. It provides a sales advantage for the marketplace, too, because properties of such products as shampoos, aerosol shaving creams and hand lotions can easily be tailored and changed to meet consumer preferences.

Finding the right emulsifying agent is no problem when Dow triethanolamine (TEA) is at hand. So versatile is TEA that this one chemical can replace stocks of many different specialized agents. But it really shines when it comes to improving product properties. In changing formulas, or in developing new ones, wide-range emulsifiers made from TEA provide exact, easy control of emulsion viscosity; at the same time they produce mild emulsions with neutral pH that are easy on the skin.

TEA-soaps produce creams of fine texture and consistency when emulsifying such ingredients as mineral oils, petrolatum, lanolin, vegetable oils and beeswax. Though the effect of the ingredient is retained, the resulting preparation can quickly be removed by washing with water.

The growing trend to modified soap-based formulations for hair shampoos indicates an ideal spot for the use of TEA soaps. For example, TEA oleate is widely used here because it provides excellent cleansing action and high stability of the emulsion. Not incidentally, it greatly simplifies manufacturing operations.

Aerosol shaving creams, too, get a boost from TEA soaps. Low alkalinity means they're noncorrosive to pressurized containers; more important, they won't irritate the skin. These emulsions of oils, lanolin, etc., provide excellent softening, wetting and lubricating action. Shaving creams formulated with a combination of TEA stearate and TEA cocoate have found ready consumer acceptance. And such formulations can be superfatted using an excess of stearic acid.

The emulsion characteristics of TEA-

Triethanolamine soaps speed the manufacture of soap-based products while improving salability and profits.

based hand lotions can be varied to give any desired texture and consistency. And they have the appearance and feel that the customers want—white, unseparating on the shelf, softening and soothing to the skin, readily removed by washing with water.

In the formulation of any soap-based product, a wise first step is the consideration of high quality TEA from Dow. Dow offers valuable Technical Service assistance to pharmaceutical and cosmetic manufacturers in developing special formulations of all kinds. If you have a problem in formulation, consider TEA from Dow. For more information on this versatile chemical, write for a copy of Dow's new booklet "Alkanolamine Soaps in Emulsions".

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Dow's new plant at Plaquemine, Louisiana, recently went on stream. This extensive new production facility means there is now plenty of propylene glycol USP available to fill industry's needs.

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. . . *save face and profits*

Drug and cosmetic manufacturers rely on Dowicide preservatives to keep shelf goods factory-fresh.

You can count on Dowicide® products to help save your product face . . . and your profits . . . when shelf spoilage threatens. Cosmetics and pharmaceuticals subject to attack by bacteria and fungi can be kept clear, clean and attractive to the shopper when one of these preservative chemicals is in the package! Among Dow's fourteen special Dowicide products there's sure to be one which will solve your preservative problem. For example, Dowicide A or Dowicide 1 are highly effective against spoilage organisms, have a low order of toxicity and irritation.

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* * * *

If you're looking for a way to brighten your sales picture, chances are there's a Dow chemical which can help you throw some light on the subject. For more information, write THE DOW CHEMICAL COMPANY, Midland, Michigan, Chemicals Merchandising Department 922AW12.

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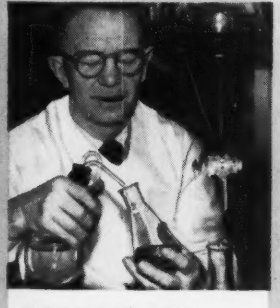


DOWANOL® DPM
Dipropylene glycol methyl ether makes an ideal coupling agent for cosmetic preparations. Toxicity is low, solvent action high, profit performance excellent.

METHOCEL®
Methocel has recently become available in new granular form. This thickener, dispersant, emulsifier, and stabilizer is tasteless, odorless and colorless.

AROMATICS
These aromatics are stable and efficient, provide a wide selection of odor raw materials. For example; Dorisyl®, coumarin, Rosaryl®, C•64®, and allylcyclohexanepropionate.

MIXED IPA
Mixed isopropanolamine is an ideal emulsifying agent for cosmetics. It protects against skin irritation and produces creams of good texture, consistency and good color stability.

Subtle superiorities

produce dramatic differences for Emersol

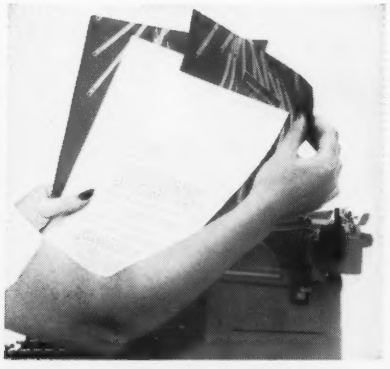
Are oleic acids pretty much alike? Basically, yes! But the subtle performance advantages of Emersol Oleic Acids do contribute to a superior product for many manufacturers . . . a product that meets a tighter quality standard and enjoys a significant sales edge at the retail counter. And, these are *bonus* performance features because Emersol Oleic Acids cost no more than other oleics of the same grade. See if these special Emersol qualities interest you.

IN VINYL PLASTICIZERS . . . *Because interior decor* is an important factor in selling cars, many producers of vinyl automotive upholstery incorporate an epoxidized oleic ester plasticizer in their formulations to keep their clear vinyls transparent and unyellowed, their white vinyls really white, and pastel colors pure and true. And many plasticizer producers have learned through experience that the lightest colored epoxidized oleic esters are made from color-stable Emersol Oleic Acids.

Oleic Acid users

IN SYNTHETIC LATEX... *Foam rubber* gets an extra lift from Emersol 233, thanks to its *exceptional purity.* Synthetic rubber latex producers find that the low polyunsaturant content of Emersol 233 imparts the best emulsion stability before final processing, provides better frothing, and keeps production uniform from batch to batch. And the consumer gets a pillow with a finer, more uniform cell structure and no objectionable odor.

IN TEXTILES... *Manufacturers of textile processing* materials such as wetting agents, rewetting agents, and softeners, are most discriminating about the brand of oleic acid they select. The heat used during processing tends to discolor any oleic acid, but Emersol Oleic Acids, with their high degree of *color stability,* offer maximum resistance to such darkening. Cotton finishers find that processing agents based on Emersol Oleic Acids keep their white goods "fresh white", which, after all, is the way the customer wants them.



IN DUPLICATING MATERIALS... *It used to be that carbon paper,* with common oleic acid as a dyestuff-solvent, developed an unpleasant personality during storage. Over a period of time, the oleic component could turn rancid and cause secretarial noses to turn up in disapproval. But now, most major manufacturers have found out about the exceptional *rancidity resistance* of Emersol 233 Oleic Acid. Many won't specify any other. And no wonder—Emersol 233 encourages repeat sales and costs no more than other oleic acids of same grade.

IN TOILETRIES AND COSMETICS... *Shelf life problems* are a major concern for producers of shampoos and other toiletries unless they contain an oleic acid with excellent *oxidation stability,* which happens to be one of Emersol 233's most outstanding characteristics. This ability to resist attack by air, even for long periods, minimizes changes in product color, viscosity, odor and texture. First-class toiletry manufacturers consider Emersol 233 LL Oleic Acid imperative for protection of their valuable brand names.

We'd like to have you prove the superior performance features of the Emersol Oleic Acids to yourself. Won't you write now to Dept. D-12 for a 20 page treatise on oleic acids, or a sample of: Emersol 233 (low linoleic); Emersol 220 (double distilled); Emersol 213 (single distilled); or Emersol 200 (undistilled)?

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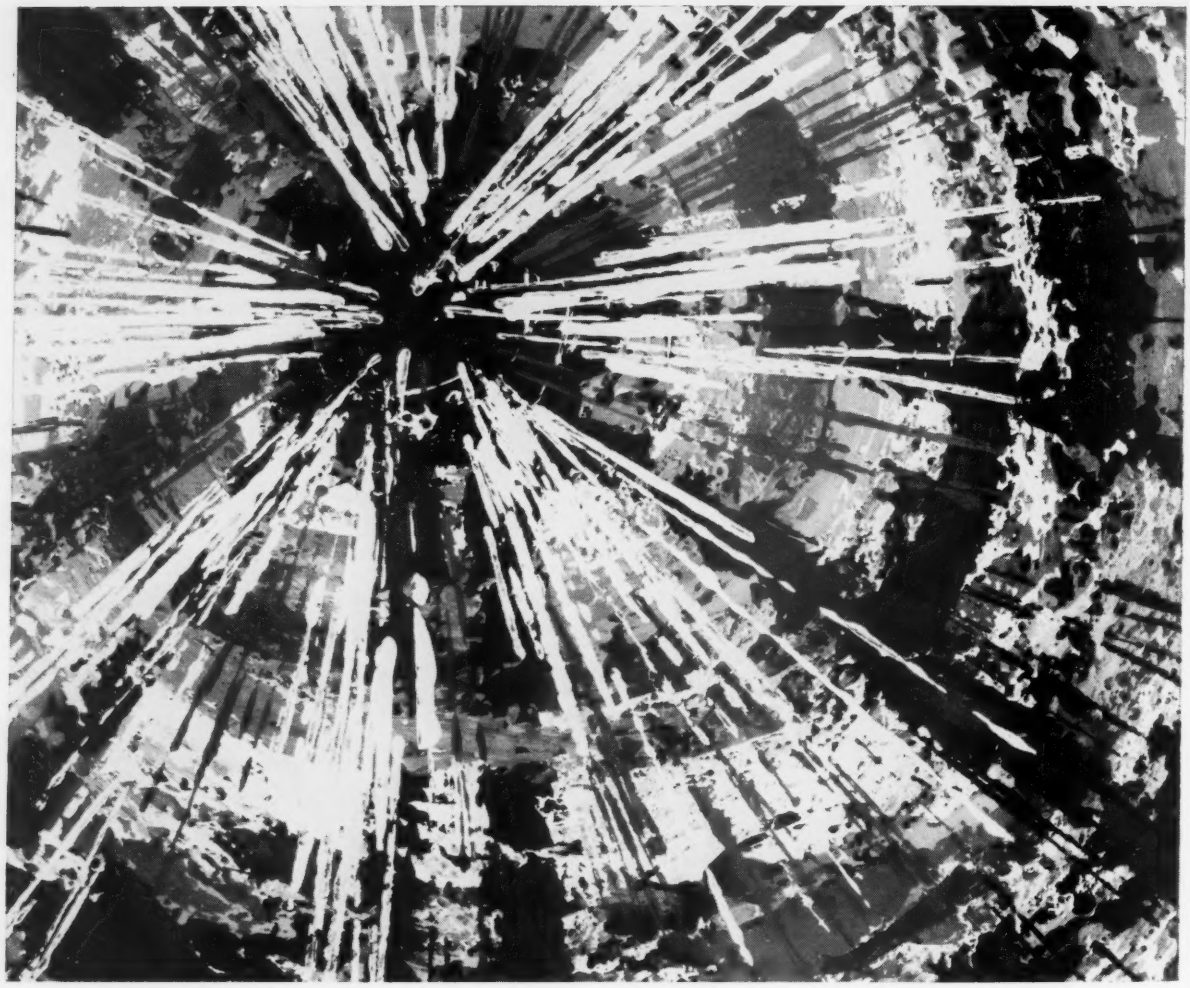

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Conoco U.S.P. SHEROLATUMS® range in color from the purest white to amber. They are odorless, tasteless . . . do not sweat . . . are free from sulphur compounds . . . will not become rancid . . . they are nondrying . . . and they will not become sticky or gummy. They are free of resinous impurities, and have low acid-forming tendencies. They are closely controlled in all steps of manufacture and distribution. SHEROLATUMS are also available in technical grades.

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Check through the list shown here, which gives you the subjects of booklets and bulletins we have published during the past 24 months . . . resulting from Atlas' own lab work. Write for any you want. And keep your eye on Atlas for important contributions, of industry-wide interest, to the art of formulating profitable cosmetics.

Guide to the use of SORBO® and surfactants in cosmetics—36 pages
Formulary of typical cosmetic formulations—32 pages
Catalog of Atlas Products for Cosmetics—12 pages
Atlas Marketing and Technical Service Bulletins on:
Anti-Perspirant Sticks, Silicone Hand Cream
Waterless Hand Cleaners, Aerosol Toothpastes
Suntan Preparations, Nitrogen-Propelled Emulsions
Using Glycerol Monostearate, Acid-Stable in Creams and Lotions
Using Glycerol Monostearate, Non-Self-Emulsifying in Soap-free and Soap-type Products
Emulsions in Flexible Containers

Chemicals Division
ATLAS POWDER COMPANY
Wilmington 99, Delaware

★*Advt. No. 2050-C—1 page, 2 colors—Drug & Cosmetic Industry—December, 1959*

"Gotta check everything in making top-grade fatty acids!"

Fatty acids that meet a user's demanding specifications shipment after shipment are essential to the manufacture of consistently fine end products. Constant vigilance by the fatty acid producer is the only way to give the user what he needs in a raw material.

Even the most carefully selected fats and oils may vary considerably in composition as received. Therefore, the maintenance of product quality and uniformity in the fatty acid plant depends on controls and adjustments at each step of manufacture. Visual and analytical laboratory tests must be made on the material in process from beginning to end.

These tests furnish a guide whereby the material is cut and trimmed by removal of impurities, volatiles, residues and color bodies—until the finished product fits the desired specifications.

Laboratory tests are translated into plant control by suitable adjustments of pressure, temperature, vacuum and flow rates in order to expedite removal of all undesirable constituents from the material in process. Manual adjustments and controls are inadequate for the continuous separations taking place. Automation is the only answer. Only by the proper combination of indicator-recorder-controllers, flowmeters and motor valves is it possible to make the minute adjustments necessary for the removal of undesirable components. These adjustments must take place minute by minute, hour by hour, day and night.

Stainless steel and aluminum pumps, lines, valves and tanks must be used in processing and storage. Containers—if they are steel drums—must have baked-on liners impervious to fatty acids. Paper bags and fiber drums impregnated with special lining materials serve the same purpose. And of course the user, too, must handle the fatty acids received with care.

A. Gross & Company has been exercising this care in the manufacture of fatty acids since these compounds were first introduced commercially. The systems and safeguards developed over the years in the A. Gross plant, to assure exact adherence to demanding specifications, have helped to build A Gross' reputation as a producer of top grade fatty acids. For information on A. Gross fatty acids such as **Groco Heat-Stable Red Oils & White Oleines,** send for the brochure "Fatty Acids in Modern Industry."

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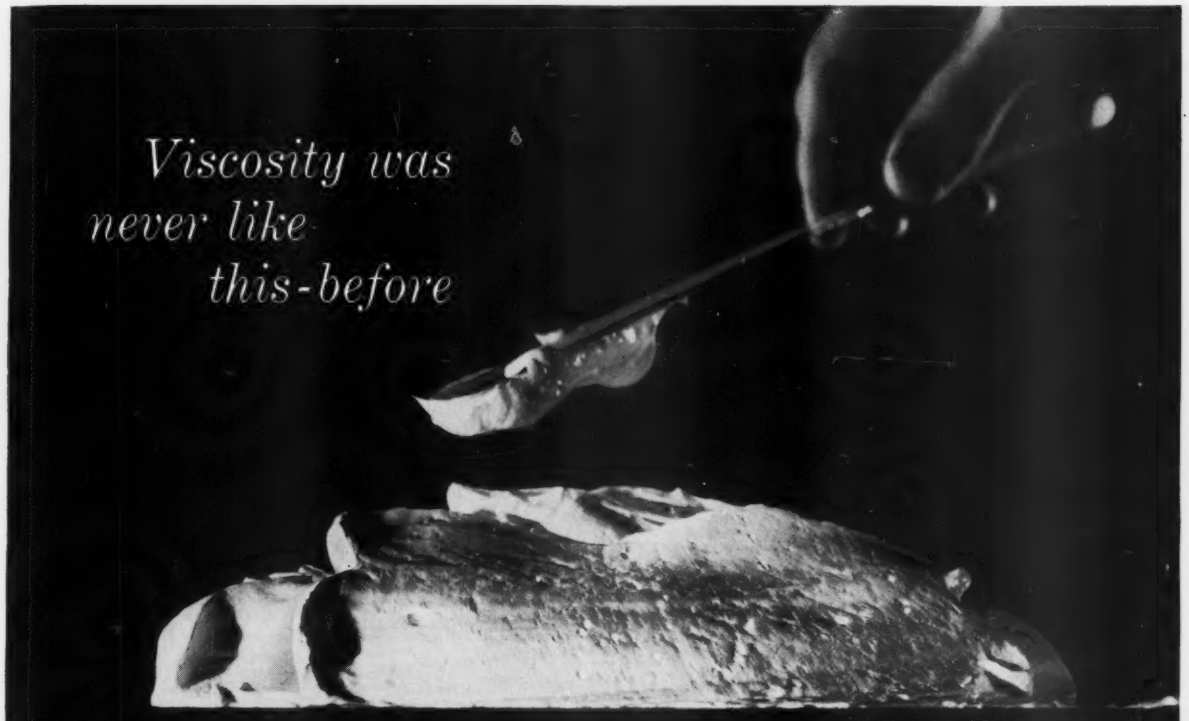
News about

B.F.Goodrich Chemical *raw materials*



LOOK HOW CARBOPOL® THICKENS A LATEX!

This photo shows a really remarkable new kind of viscosity you can get by thickening latices with Carbopol, the new water soluble resin from B.F.Goodrich Chemical. Carbopol makes a latex sit up like whipped cream—even when water content may range as high as 90%. Yet, the thickened latex is easy to spread, easy to handle.

You get better control over penetration and coating thickness. You can make a really thick latex that spreads easily to form a heavy coating, or a skin-thin coating. Latices thickened with Carbopol are compatible with a broad range of compounding ingredients.

For information on how Carbopol can improve thickening of latices for you—or samples of the material—write Dept. DB-6, B.F.Goodrich Chemical Company, 3135 Euclid Avenue, Cleveland 15, Ohio. Cable address: Goodchemco. In Canada: Kitchener, Ontario.

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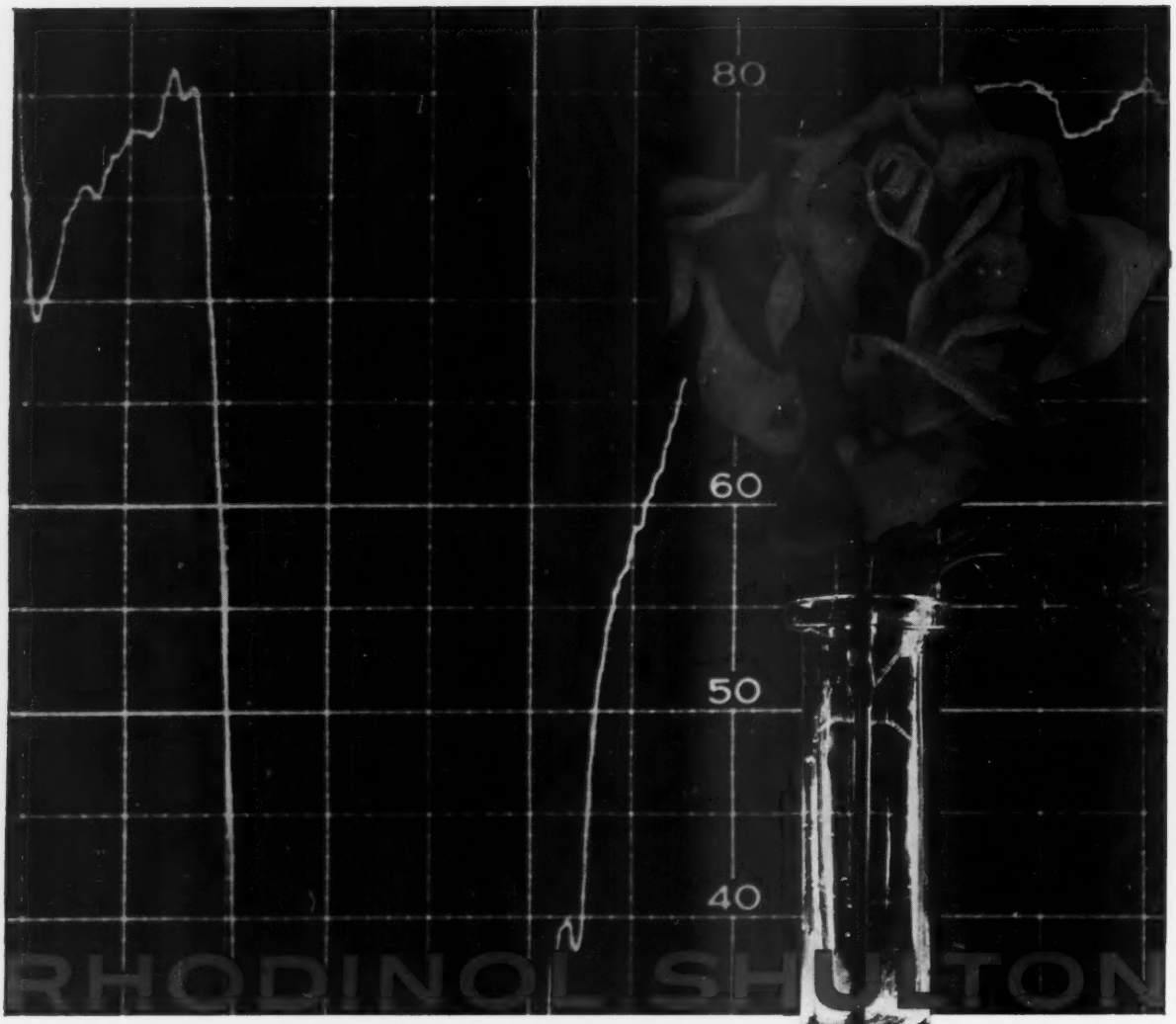
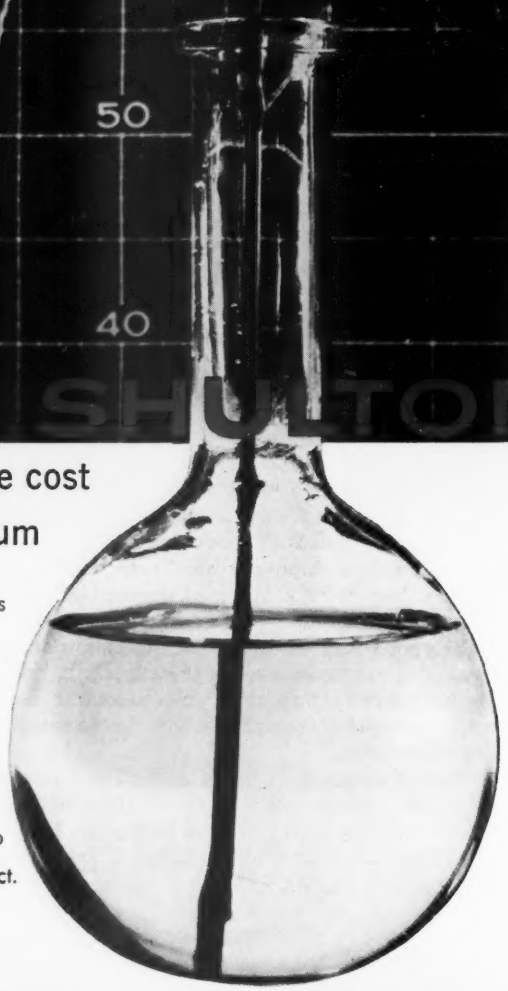


superb rose effects at half the cost of rhodinol ex-geranium

Rhodinol Shulton is superior to ordinary rhodinols in its freshness effect . . . its blending power . . . its compatibility with the finest perfume materials . . . and its stability in soap. • Shulton's advanced research combined with the perfumer's artistry makes possible this rhodinol of finest quality and constant character. And you can rely on the quality of Rhodinol Shulton because it is free of impurities, free of batch-to-batch variations. • Specify Rhodinol Shulton to procure these superb rose effects at only half the cost you might expect.



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Mylase 100 is an *a*-amylase ten times stronger than ordinary diastases derived from Aspergillus oryzae. Its high activity-to-weight ratio makes feasible pharmaceutical formulations previously limited by excessive ingredient bulk.

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Mylase 100 is standardized at 191,000 Wallerstein Units of *a*-amylase activity. Just one gram dextrinizes 4.2 pounds of soluble starch. In terms of correctives for dyspepsia, digestive insufficiencies, or just plain overeating, *Mylase 100 can give your products a diastatic effect never before attainable.*

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For superfatting of creams use

CETIOL V*

a natural oil consisting of oleic acid esters
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"Take that cold to the movies where it'll do the most good."

Keeping Posted

Colgate Buys Lakeside Labs.

Colgate-Palmolive Company is acquiring Lakeside Laboratories in exchange for Colgate stock. The transaction will result in the issuance of about 1¼ shares of Colgate stock for each share of Lakeside stock outstanding, involving about $13 million at the current price of Colgate stock. The acquisition marks Colgate's entry into the ethical drug field as announced earlier this year by Colgate board chairman and president Edward H. Little.

Lakeside Laboratories, Inc., Milwaukee, was founded in 1924. Lakeside drugs prescribed by doctors are for heart conditions, mental depression, anemia, asthma, and gastrointestinal disorders. A major share of present sales is represented by specialties, nine of which were developed in the company's own laboratories during the last seven years. Lakeside's 1958 sales were over $6 million, and the products are sold in 62 countries.

Lakeside will operate as a wholly owned subsidiary of Colgate. No changes are contemplated in Lakeside management, personnel or operations, except that Evan P. Helfaer, who has headed the company since 1932 and is now president, will become chairman of the board of the new Colgate subsidiary.

"Bonamine" Changed to "Bonine"

Pfizer Laboratories has changed the trade name of its anti-nausea drug from Bonamine to Bonine. This is the result of the court action brought against Pfizer by G. D. Searle & Co., in which Searle claimed that the trademark Bonamine was an infringement of Searle's trademark for a similar product, Dramaine. The courts upheld the Searle contention.

Miracle Doctor or Miracle Drug ?

"About one-third of the effectiveness of many modern drugs still depends upon the personality of the physician," says Dr. Edward F. Domino, pharmacologist at the University of Michigan Medical Center, who adds, "If a patient desperately wants relief and trusts his physician, he sometimes can get as much relief from a sugar tablet as from a drug. . . . It also demonstrates one of the most beautiful qualities of the physician—an almost magic ability to do great good for his patient through the force of his own personality. This is an important part of being a doctor." Dr. Domino says that between 15 and 58 per cent of the measurable effectiveness of many drugs must still be credited to the so-called "placebo effect."

It was Napoleon's Pituitary

A British physician has traced the downfall of Napoleon not to Waterloo but to the Emperor's unruly pituitary gland. In *Napoleon Immortal*, published in London late last month, Dr. James Kemble traces the medical history of Napoleon, saying:

"At 40, at the summit of his career, I think he undoubtedly became the subject of Frochlich's disease. His pituitary gland failed him prematurely; and the failure of that tiny gland changed the events of all his future years."

Dr. Kemble said the record pointed to spells of inactivity by Napoleon, his indecision, and the moral and physical prostation for which he was severely criticized. All of it was a result of the onset of the disease.

Aziza Eye Cosmetics to Chesebrough

Chesebrough-Pond's is acquiring the Aziza Eye Cosmetics Division of Mauvel Ltd., through an exchange of stock. The line of eye cosmetics will be merged into Prince Matchabelli, Inc., operations, adding a "new dimension to our Prince Matchabelli perfume and fragrance business." The Aziza line includes eye

WAVEMASK 30

works magic with home permanents

The new Synfleur fragrance WAVEMASK 30 can help cure even your most difficult case in home permanent formulation.

WAVEMASK 30, based on essential oils and aromatic chemicals, carefully tested for stability, compatibility and solubility, is an artistic formulation developed out of long and intensive Synfleur research.

In practical application, it has proven itself as practically a panacea to cold wave preparation odor problems. Additionally, it can be adapted as a basic fragrance for effective use in other thioglycolate products requiring similar masking treatment.

The Synfleur laboratories staff will be glad to assist you on your masking problems with samples, data or other help, without obligation.

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New York Sales Office Telephone Plaza 7 1960

shadow, eye creme, eyelash and eyebrow pencils, eyelash curlers, and other eye cosmetics.

This acquisition is the third by Chesebrough-Pond's in four years. In August 1956 the company bought Seeck & Kade, makers of Pertussin, and in September 1958 it bought Prince Matchabelli from Vick Chemical Company.

Washington Fair Trade Act Invalid

The fair trade act of the State of Washington has been declared unconstitutional by the Supreme Court of that state. This means that there are only 30 states in which fair trade is now effective. These states are: Alabama, Arizona, California, Connecticut, Delaware, Hawaii, Idaho, Illinois, Iowa, Maine, Maryland, Massachusetts, Minnesota, Mississippi, Montana, Nevada, New Hampshire, New Jersey, New York, North Carolina, North Dakota, Ohio, Oklahoma, Pennsylvania, Rhode Island, South Dakota, Tennessee, Virginia, Wisconsin, and Wyoming.

In 16 states the laws are not enforceable either, because the non-signer provision or the entire act has been declared unconstitutional. These states are: Arkansas, Colorado, Florida, Georgia, Indiana, Kansas, Kentucky, Louisiana, Michigan, New Mexico, Oregon, South Carolina, Washington, and West Virginia.

Four states—Alaska, Missouri, Texas and Vermont —as well as the District of Columbia, never had a fair trade act.

Lipstick Colors

The matter of certified colors for lipsticks became somewhat obscured last month by the matter of the cancer-causing weed-killer that was found in some lots of cranberries. Secretary of Health, Education and Welfare Flemming had no hesitation in backing up the Food and Drug Administration in siezing contaminated lots of berries and throwing a general scare into the public so that, for a time, it looked as though no cranberries would be available for Thanksgiving. It looked very much as if an attempt was being made to prove the unworkability and unfairness of the Delaney cancer amendment to the Food Additives legislation, and probably that was the purpose. However, it seems that the public attitude to this amendment was very favorable, and now the Secretary has declared that he will oppose any attempt to take the cancer provision out of the Food Additives Amendment, and that he will support the inclusion of such a provision in the color legislation now before Congress. He further declared that the cranberry situation illustrates the FDA attitude in declining to set any tolerances for any amount of a chemical in foods if the chemical produces cancer when fed to test animals.

When the cranberry story was at an end in the daily press, the lipstick color situation was generally aired. And, following the cranberry success of FDA, it looked as though the Department was becoming tougher in its attitude toward colors. There seemed to be an attitude on the part of the FDA to refuse any hearing on the subject of delisting the colors early in January as requested by the industry.

The FDA recently won a unanimous decision in the Eighth Circuit Court of Appeals which upheld the right of FDA to dismiss appeals from its color delisting orders without hearings, despite regulations which might state the contrary.

The case involved the delisting of colors and, during the period of 90 days before the delisting became effective, the U. S. Supreme Court decided against tolerances for colors in the Florida Citrus Exchange case. Since the claims for review at a hearing were of such a nature that they were based on tolerances, the FDA refused a hearing. The colors were not "harmless," and that was that. This refusal of a hearing was upheld by the court.

The same situation could prevail in the lipstick colors case if the plea for a hearing is based on the fact that the colors are harmless only as used, when the FDA has found them to be harmful when fed to animals in amounts much greater than in lipsticks. The fact that they are harmful in any amounts and under any conditions is sufficient for the FDA to delist them under the law. So why hold a hearing?

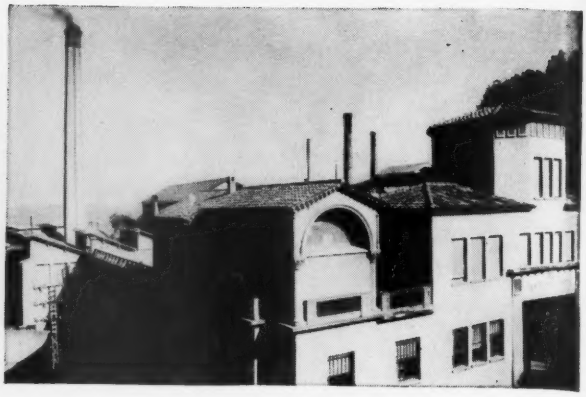
The Pharmaceutical Manufacturers Association, which also is interested in these colors because of their use in pharmaceutical products, in its request for a hearing, maintains, among other things, that: "the FDA admits that it has not tested all of the colors proposed for delisting, assuming that other metallic salts will behave similarly to those tested. With respect to new drug applications, the Administration has never permitted companies to omit all tests on different salts of therapeutic agents, and we feel that such requirements should apply to the government as well as to private citizens."

PMA Award to Dr. Long

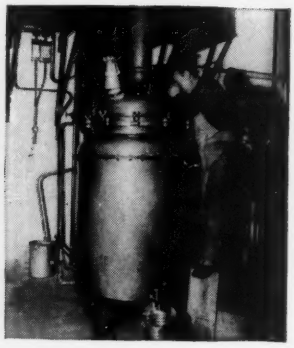
Dr. Cyril N. H. Long, Sterling Professor of Physiology at Yale University School of Medicine and its former Dean, is the recipient of the 1959 PMA Award. He was the unanimous choice of the Award Board of Edward Henderson, chairman; E. L. Burbridge, Benjamin W. Carey, Robert Cutter, George Hazel, John Henderson, Raymond Rice, George P. Rieveschl, Jr., W. Furness Thompson, Max Tishler, and I. C. Winter, with board chairman William B. Graham and President Austin Smith concurring.

SKF Buys Norden Laboratories

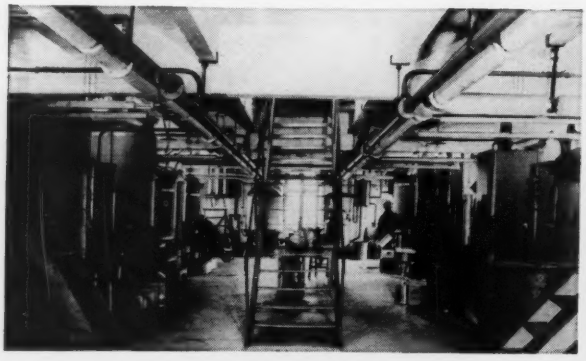
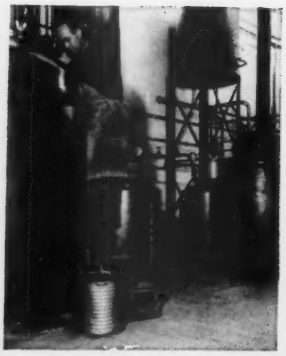
Smith, Kline & French Laboratories is purchasing Norden Laboratories, Lincoln, Nebraska, manufacturer of veterinarian pharmaceuticals and biologicals, on a basis of three and one-half shares of SKF stock for one share of Norden stock. SKF will acquire the assets and liabilities of Norden. The acquisition



CAPACITY



QUALITY

for the finest in floral and essential oils

BERTRAND FRÈRES, INC.
443 FOURTH AVE. NEW YORK 16, N.Y.

will give SKF an established position in the veterinary field and provide a new market for certain of its products. Norden laboratories, which will continue as an SKF subsidiary, will receive promising compounds from SKF research operations for development and marketing in the animal health area.

Charles of the Ritz Buys Venus Pencil

Charles of the Ritz, Inc., is acquiring 100 per cent of the closely held stock of the Venus Pen and Pencil Corporation. A joint statement by Richard Salomon, president of Charles of the Ritz, and Richard Lewisohn, president of Venus, said that Venus will be operated as a wholly owned subsidiary of Charles of the Ritz, with all present Venus executives continuing in active management, and with trade policies and manufacturing operations maintained as heretofore.

Mr. Salomon stated that the acquisition of Venus is another forward step in the corporate growth and diversification of Charles of the Ritz, whose sales have increased 150 per cent in the past five years. The 98-year old Venus Pen and Pencil Corporation, which has tripled its sales volume in the past five years, manufactures more than 2,500 products in its lines of writing instruments and toys, and is the only company in the U. S. producing a complete line of pens as well as pencils.

Charles of the Ritz doubled the number of its company-owned salons to 22 in the last five years, and has acquired Alexandra de Markoff Sales Corporation and Anatole Robbins Corporation.

Carter's Little Pills Lose "Liver"

After battling the Federal Trade Commission for 16 years, Carter Products has finally lost the right to use the word "liver" in the name of their famous Carter's Little Liver Pills. The final action occurred November 9, when the U. S. Supreme Court refused to review a decision handed down on June 16 by the U. S. Circuit Court in San Francisco upholding a 1956 FTC order which had been upset by a previous appeal to the U. S. Supreme Court by Carter.

Soap and Detergent Sales Up

Soap and synthetic detergent sales set a new record for both pounds and dollars in the first nine months of 1959, according to reports of 62 manufacturers to the Association of American Soap & Glycerine Producers. Sales of soap and synthetic detergents totalled 3,236,700,000 pounds valued at $830,222,000, up 4.7 per cent and 5.5 per cent, respectively, from the first nine months of 1958.

Synthetic detergents totalled 2,423,099,000 pounds, valued at $586,071,000, up 7.6 per cent in pounds, and 5.6 per cent in dollars. Solid synthetic detergent sales totalled 2,000,699,000 pounds, valued at $433,755,000, up 4.1 per cent in pounds, and 0.4 per cent in dollars. Liquid synthetic detergents totalled 422,400,000 pounds, valued at $152,316,000, up 28.2 per cent in pounds, and 23.9 per cent in value. Synthetic detergents now constitute 74.9 per cent of all sales in pounds, and 70.6 per cent in value.

Soap sales were 813,601,000 pounds, down 3.2 per cent, but dollarwise sales increased 5.2 per cent to a total of $244,151,000.

Scouring cleanser sales, not included in the above figures, totalled 292,834,000 pounds, valued at $40,831,000. No comparisons are available.

FTC Cites Colgate "Protective Shield"

The "protective shield" television ad for Colgate Dental Cream is deceptive, the Federal Trade Commission charges in a complaint against Colgate-Palmolive Company. According to the Commission, the dentifrice does not completely protect users' teeth against tooth decay or the development of cavities by forming a "protective shield," or otherwise.

Colgate Toiletries Expansion

Colgate-Palmolive Company is engaged in a major construction program for the Toilet Articles Division at its Jeffersonville, Indiana plant to speed up service for the midwest and south. The project, which is costing more than a million dollars, includes a four-story addition to the present toilet goods manufacturing building, a two-story addition to the toilet articles packaging and shipping center, a new two-story warehouse for supplies and finished products, and a one-story office building for Toilet Articles plant manager C. J. Slaton, and his staff.

Toilet articles made at the Jeffersonville plant are Colgate Dental Cream, Colgate and Palmolive shaving preparations, Halo Shampoo, Lustre-Creme Shampoo, Veto Deodorant, and Cashmere Bouquet Talc and Hand Lotion.

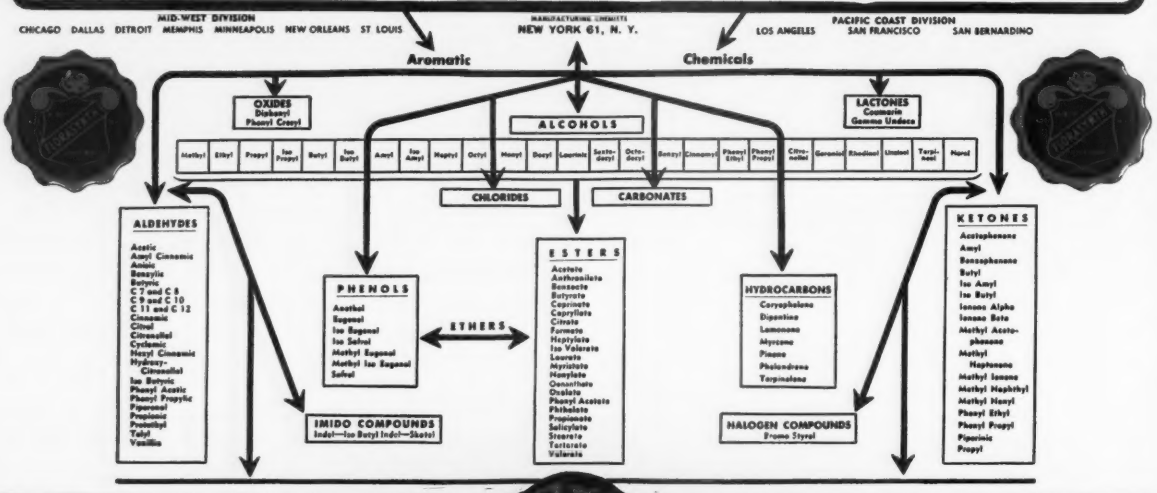
Journal of Nuclear Medicine

The Journal of Nuclear Medicine is a new quarterly publication of the Society of Nuclear Medicine, the first issue of which will appear in January 1960. Editor is Dr. George E. Thomas of St. Louis; associate editors are Titus C. Evans, Iowa City; Niel Wald, Pittsburgh; and Eugene L. Saenger, Cincinnati. The editorial content will be directed toward those members of the medical and allied professions who are interested in the diagnostic and therapeutic application of radioisotopes and in human radiobiology. Annual subscription is $10, from the publisher, Samuel N. Turiel & Associates, 430 N. Michigan Avenue, Chicago 11, Illinois.

Toni's Expanded Research

The Toni Company last month dedicated its expanded research laboratories in the Merchandise Mart, Chicago, largest in the world devoted to the study of cosmetic products for use on hair and skin. In 1960 The Toni Company will allocate a record

FLORASYNTH LABORATORIES, INC.



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St. Louis • San Francisco • Boston
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$2 million for its laboratory activities, making the company one of the leading spenders, if not the leading spender in this category among all cosmetic companies.

Raymond E. Reed, vice-president in charge of technical operations, points out that the dedication marks the completion of a two-year expansion program in the company's research department. The program involved doubling of Toni's Chicago research facilities, acquisition of much new, valuable and unique laboratory equipment and a substantial increase in division's technical staff. The research staff consists of about 200 scientists and technicians under the direction of Mr. Reed and Dr. Ray C. Houtz, director of research. The largest in number are chemists specializing in organic, inorganic, physical, analytical and biochemistry. Others include histologists, biochemists, microscopists, physicians, statisticians and dermatologists.

The objectives of this group are "to insure medical, chemical and physical safety and efficacy of products; to make these products esthetically attractive and pleasing; to maintain quality and product uniformity; to improve present products and to develop new products and processes." The scope of their research activities includes toxicological studies on animals, dermatological patch tests on humans, off-the-head tests on human hair, testing under practical use conditions with live models.

"Today, technical research plays an ever-increasingly important role in the development and testing of cosmetic products, prior to their introduction to the public," say Vice-President Reed. "Voluntarily, Toni applies the same rigid standards to its products as those exercised in the development and manufacture of pharmaceutical products. Prior to national marketing, every one of our products undergoes intensive scientific research, market and consumer testing, before it is offered for national use. . . . In the cosmetic industry, appreciation of the need and value of research has grown steadily. The Toni Company has always utilized extensive scientific study in the marketing of its products. Today, it sets the pace among companies in its field and is recognized as the world leader in hair research."

Additional Toni research activities are conducted at a number of other localities. The laboratory connected with the Toni plant in St. Paul, Minnesota, maintains extensive controls to insure product purity and uniformity and researches new production processes. As a division of the Gillette Company, Toni participates in the research experience on hair and skin of other divisions in Boston, Montreal, and London, England. Harries Research Laboratories in Washington, D. C., a division of Gillette, handles scientific programs in the fields of fundamental keratin and detergent chemistry. In addition, other studies are conducted regularly at various universities, including Notre Dame, Northwestern and the University of Illinois.

Most of Toni's research work is carried out in the Chicago laboratories, where studies are directed toward the physical and chemical study of hair and skin and the effects upon them of various products and processes. New chemicals are synthesized; experimental formulations are prepared and tested; competitive products and methods are evaluated.

A large beauty clinic also is maintained in the Merchandise Mart, where experimental waves and shampoos and other tests are conducted on thousands of women volunteers each year.

Parke, Davis Building in Italy

Parke, Davis & Company has begun construction of a combined manufacturing and sales branch in Milan, Italy. The company has had a manufacturing and sales branch in Rome since 1955, which it plans to retain as a supply depot to expedite distribution of pharmaceuticals throughout Italy, but is investing about $1 million in the Milan installation to meet the continued growth of the Italian market.

The new production unit and administrative office buildings are being erected on a 15-acre tract near the Milan airport, about eight miles from the center of the city. The two buildings will have a total of 54,000 square feet of floor space, and will employ about 100 persons, mostly Italians.

FDA Increasing Vigilance

The Food and Drug Administration is planning to give closer supervision to claims for therapeutic values of new drugs and the promotional efforts of manufacturers and distributors. The increased activity is part of a program now being worked up by the government to improve conditions for the older part of the population. FDA will introduce new legislation that will apply the principle of pretesting for safety to new drug and therapeutic devices that are coming on the market. FDA's efforts toward a solution of some of the problems related directly to the older age group was outlined in a report made to the President by the Federal Council on Aging. Pointing out that FDA must approve every new drug before it appears on the market, and therefore the agency is in a position to give tremendous assistance to the aged, the report says:

"More and more new drugs are being developed to treat diseases of older persons. By the same token, more and more drugs are being developed to cope with degenerative processes. This agency must take steps to assure that such drugs are pure and potent; that they are properly labeled with adequate directions for use and, where appropriate, with warnings against misuse.

"The question of false and misleading claims represents probably one of the most difficult and imposing food and drug problems facing our older population today. Medical and nutritional quackery are on

the upswing. Both are either keeping pace with or exceeding the growth of our older population. It is among the older group that the unscrupulous operator finds the greatest potential for his wares and services. It is in this age group that we find the diseases with which medical science is not fully capable of dealing—such as cancer, heart disease, arthritis, and others.

"The promotion of special health foods and vitamins represents a growing industry in this country. Much of the promotional effort behind these products is being directed to the older population. This is another field which is wide open to cheats and frauds.

"The Food and Drug Administration is very much aware of its responsibility in these areas and is devoting more and more of its resources to these particular problems.

"It is currently in the process of improving and strengthening the review and approval of new drug applications. It is about to embark on a limited program directed toward the evaluation of new devices some of which are being developed for marketing among older persons.

"The Food and Drug Administration has done some limited research to evaluate the nutritional qualities of health foods and vitamins. A recent series of court cases against a well-known but fake cancer cure has been conducted.

"It is the objective of the Food and Drug Administration to direct more and more of its efforts to these particular problems, and as additional resources become available, FDA will be able to increase its vigilance against the quack and his worthless products; will be able to increase its research in an effort to resolve more of the problems which are facing our growing older population."

Disease and Research

In addressing the American Marketing Association recently, L. D. Barney, president of Hoffmann-La Roche, Inc., set the goals of pharmaceutical research during the next ten years as follows:

"First, there are the unsolved medical problems: Cancer; arthritis; heart disease; vascular diseases, particularly those of the brain; dental disease which in spite of recent progress is still a tremendous problem; neurologic disorders; the common cold; influenza; sinus infections; hay fever; virus diseases; arteriosclerosis; high blood pressure; obesity; congenital deformities; skin diseases; and as the lifespan increases the degenerative diseases of old age will require increasing attention.

"Next, there is need for improving drugs now in use. Some will unquestionably be replaced by safer and more effective compounds. For example, there is a need for better pain-relieving drugs. There is need for drugs with more specific action—a rifle instead of a shotgun.

"Nutrition is a field where we can look forward to important advances. The same is true of preventive medicine.

"We shall be on the lookout for more economical methods of research. Some research projects are prohibitively expensive; by developing better methods of testing and screening compounds, we may be able to reduce the cost of finding valuable new drugs. No doubt there will be greater use of atomic energy in the form of radioactive isotopes.

"We shall also aim for greater convenience for both physician and patient: For instance, medication which has to be taken only once a day or perhaps even once in several days. Whenever possible, injections will be replaced by more simple methods of administration. Such new technical methods as aerosols and plastic packaging offer promise.

"Last, but certainly not least, is the search for less expensive compounds—particularly for those diseases where prolonged treatment is essential."

For success in research, Mr. Barney said that three factors are essential:

"First, talent. Research cannot be better than the people who conduct it. They must be selected with great care so that they fit into a modern research organization, they should be creative self-starters, not easily discouraged and able to participate in teamwork. However, there is also room for the lone wolf whom you encounter in the field of science.

"Second, environment. Above all, we need a good esprit de corps. As a former research director of the General Electric Company put it, the least direction is the best direction in research. We must see to it that our scientists have a minimum of paper work and a minimum of committee meetings. They should devote their time, energy and talents to creative research. We need a permissive atmosphere which enables a gifted individual to strike out on his own and to deviate from the beaten path. Researchers should feel that management appreciates their efforts even though they frequently end in failure.

"Third, and perhaps most important, is luck. But the word luck should be properly defined. Once, when Napoleon was given a list of officers recommended for promotion, he pointed at a name and asked, 'Is he lucky?' When his aide voiced surprise at this question, Napoleon said that luck was simply the ability to recognize opportunity and to take advanage of it. This is what we need in research."

Increase in Doctors

The 1958-59 graduates receiving the M.D. Degree numbered 6,860, only one less than in 1957-58. These were the largest classes except for 1954-55 when there were 6,977 graduates, a year in which there were included as graduates the 50 students completing the intern year required by Stanford University. Women comprised 5.4 per cent of graduates in this country and 5.9 per cent in Canada.

THE FLAVORING OF ANTIBIOTIC PRODUCTS

BY A. J. SPIEGEL AND M. M. NOSEWORTHY CHAS. PFIZER & CO.

Much of the literature dealing with pharmaceutical flavoring has been of a general nature.[1-6] These reports serve as a good background for work in this field, as do the flavor guides published by several flavor manufacturers.[7-10]

Interest in the field of flavoring has been increased by the holding of symposia dealing with the Chemistry of Natural Food Flavors, sponsored by the Army Quartermaster Corps,[11] and Flavor Research and Food Acceptance, sponsored by Arthur D. Little, Inc.[12]

Several authors have reported on the flavoring of specific antibiotics,[13-17] but the entire antibiotic field has not been surveyed. Thus, our aim is to present a detailed report on the flavoring of antibiotic products, discussing the efficacy and acceptability of various flavoring combinations, methods of evaluation, and specific recommendations.

When considering a new formulation problem, the pharmaceutical flavor chemist is confronted with a series of conflicting interests and conditions. Often, specific requests from sales or marketing groups may call for a particular flavor and color combination to satisfy a preference in a local market area. An informal survey conducted by our international subsidiaries indicates geographic and ethnic preferences which limit the use of a single over-all acceptable flavor for a particular product. Table 1 (see page 846) illustrates this point.

The age of a consumer plays an important part in the selection of an appropriate flavor. For example, children prefer the sweet fruit flavors, while geriatric dosage forms are more readily acceptable if they contain tart fruit or wine flavors. Also, color and taste characteristics of a particular medicament may preclude the use of a requested combination.

Arthur D. Little[18-21] has developed a system for flavor description known as the "flavor profile." This system "presents a descriptive analysis of flavor, expressing in common language terms, the characteristic notes of both aroma and flavor, their order of appearance and intensities, and the amplitudes of total aroma and total flavor." A time-intensity flavor study method has also been described.[22]

The taste characteristics or pattern of a drug, that is, the initial tast, middle taste, and aftertaste, may also preclude the use of certain flavor groups. A product with an acid taste does not readily lend itself to the use of bland flavors such as butterscotch, caramel, or custard; rather it requires acid fruit or citrus flavors.

The pharmaceutical chemist can, by tasting the raw material, establish a "taste pattern." Initial taste is intimately related to aroma, since this is the first perceived sensation. Although most antibiotics are odorless, the penicillins do have a slight odor. The middle-taste sensation varies and includes such physical characteristics as chalkiness and grittiness. The final taste is usually most pronounced and consists of a lingering taste which, in the case of antibiotics, is usually one of bitterness.

The formulator must seek a flavoring agent or combination of such agents which will mask or blend with objectionable characteristics of the medicament.

Examples of flavor types that can be used for each taste group are: (1) initial—cherry, pineapple, raspberry; (2) middle—custards, raspberries, apricot, peach, grape, citrus; and (3) after—mints (spearmint, peppermint), floral (violet), chocolate, vanilla, spices (cinnamon). This classification is not too binding, since certain flavors can act as initial coverers in some instances or appear in the middle taste or aftertaste of another taste pattern. It is, however, a starting point.

Antibiotics, as a rule, change in color and character with time and exposure to variations in temperature. The flavors should be chosen with these factors in mind, since these agents should mask the medicament throughout its entire shelf-life.

There are within each class of flavors variations

(*Continued on page 842*)

COURTESY ELIZABETH ARDEN

MODERN COLD WAVE NEUTRALIZERS

BY J. PAUL SARENSEN
PAUL'S HAIR FASHIONS MURPHYSBORO, ILL.

Some years ago, it was axiomatic that a permanent wave was 90 per cent operator-ability and 10 per cent permanent waving equipment, or supplies, such as chemicals and neutralizers. This last 10 per cent concerned manufacturers. Several authorities have voiced the opinion that a patron can better afford to get a bad permanent wave than an operator or hairdresser can afford to give one. With this point of view, we look at better products for the beautician and for the manufacturer.

The home permanent is big business, but the professional product in the beauty salons is no less important. Beauty operators have become wiser in the selection of products used in the salon. They not only expect better results from the chemicals or supplies used to accomplish the finished wave, but are always looking for something better or budget-priced.

Chemists test various lotions, using the *p*H meter for testing alkalinity, and determine the mercaptan percentage in thioglycolates, but the real test of the permanence of the permanent wave and of the softness of the hair after waving lies with the patron and the operator. The wave must be checked, time after time, between shampoos and pin curls. It must be checked for over-relaxation, or loss of permanent curl. Dryness and porosity are important factors here also.

Regardless of what difficulty the patron presents to the operator in the way of extra-fine textured hair, extreme coarseness of hair, and even dyed or bleached hair, the patron must be accommodated.

Today's trend is more color and more bleach to more heads of hair. Color is here to stay, and this presents more problems to the permanent wavers. We must use more lanolins, cholesterols, and opacifiers. There is, also, the problem of hair that seems to be weightless, limp, and dead in appearance. Operators are confronted daily with these dilemmas.

Assuming now, however, that ammonium hydroxide and thioglycolate combinations are used universally, for the first part of the permanent wave, let us say that these may or may not contain certain opacifiers. They are rubbed on or poured over the hair in various ways so that they may be dispersed over the rods. They change, swell, and soften the protein disulfide-linkage bonds of the hair. The operator chooses the size of the rod, determining the S-formation of the wave or curl desired for the finished

styling. The operator also decides how long this processing must go on, before neutralizing. All of this first procedure is essential for the permanent wave. But, the main part of the permanent lies with the neutralizer. For it is this last part of the wave that determines whether we have a permanent permanent wave—or a failure.

Let us go back a few years, and see what has taken place with these neutralizers. About 20 years ago, we started the cold-wave neutralization by mixing liquid peroxide, some liquid shampoo, and enough tepid water to make a pint of the finished solution. This was then poured over the curls at the shampoo bowl. It was then left on the hair about five minutes and, finally, rinsed with cold water, completing the wave.

About five years later we were concentrating on powder neutralizers packaged in aluminum foil sachets, or envelopes. They consisted of about 20 grams of sodium perborate, or ureaperoxides. These powders did the trick fairly well, while others hardened on shelf-aging. Then came the bromate fixatives; first, the potassium salt, then the superior sodium bromate. Several years ago, the quaternaries came into vogue. They too, did an adequate job, but their viscuous unguent conglomerations seemed to drag down the curls. They weakened the S-formation. This whip-like formation is what the operators look for in determining the amount of curl. However, some of these types of neutralizers are still found in supply houses and beauty salons, both here and abroad.

Here are some modern formulas used to neutralize thioglycolate-ammonia solutions.

FORMULA 1

Sodium bromate	4 oz.
Sodium perborate monohydrate	2 oz.
Sodium tripolyphosphate	1 oz.
Sulfonated castor oil	1 oz.
W. S. perfume oil	0.5 oz.
Distilled water	119.5 oz.
	1 gallon

The procedure is general, perfume is optional, and the finished product can be colored, but this is not necessary. This formula provides a good neutralizer, but is not the fastest acting, or the best.

FORMULA 2

A.	10 grams Oxone monopersulfate, sealed in packaged aluminum foil envelope.	
B.	Sodium bromate	5 oz.
	Distilled water	122 oz.
	W. S. perfume	1 oz.
		1 gallon

For use on one permanent, four ounces of hot water is mixed together with the Oxone from the envelope. Dissolve all the powder, add two ounces of liquid to this mixture, then add enough water to make one pint. Leave the mixture on the rods about ten minutes, then complete the wave by rinsing with tepid water. This is especially successful for difficult, or fine, thin hair; it may be colored if desired. Unless a bleach-fast color is used, however, the Oxone will bleach out the color upon addition to the liquid part of the neutralizer.

FORMULA 3
One-minute, One-step, Sudsy Neutralizer

Sodium bromate	5 oz.
Sodium lauryl sulfate	2 oz.
W. S. perfume	1 oz.
Ferric ammonium citrate (green)	0.5 oz.
Cetyl trimethyl ammonium bromide	0.25 oz.
Distilled water	119 oz.
	1 gallon

For this formula, the bromate is dissolved in the warmed distilled water and to this the other ingredients are added, one at a time. The cetyl trimethyl ammonium bromide does not aid in the neutralization process, but is an aid to the patron's sensitive scalp. It also helps recondition the hair.

Formula 3 is far ahead of the others on the market. It is remarkable what it can do in just a few minutes. The ferric ammonium citrate works as a catalyst in conjunction with the bromate and digs deep down, sudsing and foaming around the rods, yet it is thin enough in solution for good adsorption. This neutralizer assures permanence of the wave. Moreover, it saves much time for the operator, because of its quick astringent action on the rod. Use about three ounces of this solution with enough water to make a pint of finished neutralizer. This is poured over the curls on rods at the shampoo bowl, and should remain on the rods between one and two minutes, a procedure familiar to the average hairdresser. This neutralizer makes practically all others obsolete.

COURTESY ELIZABETH ARDEN

THE LAW AND PHARMACEUTICAL ADVERTISING*

BY RAYMOND D. McMURRAY, GENERAL COUNSEL, HOFFMANN-LA ROCHE, INC.

In addition to the Federal Food, Drug, and Cosmetic Act, several other federal trade regulations acts, and such agencies as the Federal Communications Commission, which help to insure a straightforward approach in advertising, codes of self-regulation have been adopted, and are embodied in the "Statement of Principles of Ethical Drug Promotion" of the Pharmaceutical Manufacturers' Association, and the "Code of Ethical Practices in Proprietary Advertising Copy," published by The Proprietary Association.

Along with these regulations goes the fact that advertising can be a source of grave trouble if approached in an irresponsible manner. In order to catalog only a few of the major sources of possible conflict between ourselves and others, I have selected certain legal pitfalls which seem to be favorites of our antagonists.

One of these is fraud and misrepresentation. This might include a misstatement relative to ingredients or potency, or quality, or therapeutic value. Fraud can occur through a positive statement, through a negative statement, or through the lack of any statement where one is indicated. Fraud can occur when our duty to warn of certain dangers inherent in the product has knowingly not been met. Fraud in its several aspects can be the source of an action by the Justice Department or another federal agency, by state or local regulatory authority, or by any injured party under a statute giving that party a cause of action, or, finally, in many instances by an injured party under a common law right violated by the fraud.

Libel and slander represent another tender area of possible legal liability in pharmaceutical advertising. Alleged derogatory remarks, printed or spoken, photographs or drawings which hold the subject up to ridicule, or misstatements or exaggeration of facts can lay the groundwork for a suit against the corporation by an aggrieved party. The good faith of the proponent of the alleged libel or slander is of very little value in a law suit of this nature. It is the fact of public ridicule or degradation which is important, and which sets the measure of damages. Releases for photographs or statements are only part of the protection that should be insisted upon in this area, and care and caution should be taken in the manner of presentation of any published reference to an individual or corporation.

There are also the laws involving unfair competition and trademark violation, and their first cousin, copyright violation. Liability in this area can embrace not only the copying of a trademark of a competitor, but also the adoption of a trademark that is deceptively similar, or perhaps only suggestive of the competitor's trademark. It can include any manner of doing business which is calculated to give an unfair advantage to one party over another in his business dealings within the trade. The copyright law and the law of literary property forbid the piracy of printed and graphic material in its original form. The advertising man might find the bogey of unfair competition raising its head if he should unfairly compare his product with a competitor's, or unfairly characterize his competitor's product, or if he should imitate the advertising or packaging or promotion of a competitor.

We should be well aware of the legal principle that allows a certain amount of "puffery." The law, in its wisdom, takes a benign attitude toward the "buy-mine-it's-the-best" approach, and certainly we

*Abstracted from a paper presented before the Pharmaceutical Advertising Club, November 1959.

are all loyal enough to believe that we really have the finest product available, and that the public should be so informed. But knowing that we are allowed to do this is a knowledge fraught with danger, and one which requires, at times, a very careful decision as to where puffery ends and where fraud, misrepresentation, or unfair competition begins.

Pharmaceutical advertising, in addition to its other features, is peculiarly susceptible to regulations of the Post Office Department, which forbid the mailing of lewd or otherwise objectionable written or graphic material. Fortunately, the Post Office takes a reasonable attitude toward the dissemination of various scientific data, and within the bounds of good taste and decency there is very little prohibition attached to the subject matter arising in connection with the sale or promotion of our products. Be careful not to abuse this important license. Retribution can be swift and costly.

Radio and television advertising present us with another set of rules involving the Federal Communications Commission and the Federal Trade Commission. Because of the high impact of these media, they are being watched with increasing care to avoid excesses in advertising approach. In November, Earl Kinter, the new Chairman of the Federal Trade Commission, announced that he would more than double his staff of TV advertising moniters and, in addition, it was announced that the major TV networks would cooperate by sending to Washington film strips of advertising, in order to ease the load. Radio and television, because of the present distasteful publicity surrounding their broadcasting operation, will now tend to over-comply with all applicable regulation of their industry. We must recognize the reason for this attitude on their part when placing new material with these media. I feel that the broadcasters, like those in our own industry, will eventually work themselves out of this unfavorable period, and in the end there will be no need for further federal regulation; but they must have the cooperation of their advertisers in the prevention of fraud or misrepresentation in the promotion of advertised products.

Turning for a moment to ethical advertising, I would like to mention a principle which should be self-evident, and that is that the basic document in the advertising of ethical pharmaceutical products must always be the product brochure that has been presented to the Food and Drug Administration in connection with the required New Drug Application filed in support of the product. Many companies reprint this NDA brochure in the form of a reference card or pamphlet, thus providing a basic promotion piece having a quasi-legal standing. It must be recognized that promotion which prints excerpts or condensations or interpretations of the NDA brochure runs the risk of misrepresenting a product in some manner.

Additionally, I would like to mention a little understood requirement of the Food, Drug, and Cosmetic Act which can plague the unwary or the unaware. This is the requirement that labeling include all of the information necessary for the use of the drug by the person competent to use it. The accepted legalistic approach to labeling is that it is the informative material which originates with and is calculated to come to rest at the same place as the product. Our problem is in determining when and advertisement or promotion piece is labeling, and when it is not. When must it fulfill the requirements of the law relative to labeling? Upon the determination of these questions may depend a good deal of legal liability.

As a rule of thumb, I use the following principle: where comprehensive indications and dosage instructions are given, this is labeling. It is labeling regardless of whether it appears in a journal advertisement, or a promotion piece, or a counter card, or any other selling device. Once it is determined that the particular piece is labeling, by whatever criteria you choose, then the contraindications and warnings must also appear in conjunction with the indications and dosage. There is little room for deviation. We must also recognize that, because of the duties imposed upon us by FDA labeling requirements, we run the risk that noncompliance can be a prime factor in any product liability claim.

In the face of such comprehensive regulation, it is a source of unending amazement to me that such effective pharmaceutical advertising is able to be produced so consistently within our industry. It is indeed a most difficult professional accomplishment when we take into account the additional fact of the pressure on the advertising groups from within the company itself, requiring them to meet deadlines, to accept facts and figures which they have not themselves gathered, to be bright and attractive and cheerful, in order to gain attention without appearing to be gaudy and cheap, to sell, without seeming to sell, to educate without offending.

In reviewing advertising in this field, lawyers are sometimes asked to advise on the possibility of taking a calculated risk, or to evaluate the legal effect of a questionable statement. Can there be such a thing as a calculated risk in pharmaceutical advertising? Just how far should the pharmaceutical advertiser be

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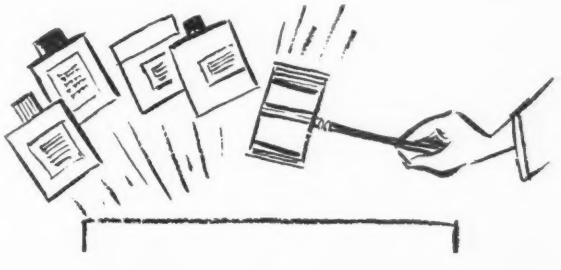

INSTRUMENTAL EXAMINATION OF AROMATICS*

BY ERNST T. THEIMER, Ph.D.
VAN AMERINGEN-HAEBLER DIVISION, INTERNATIONAL FLAVORS & FRAGRANCES, INC

The modern techniques of instrumental analysis—vapor phase chromatography for the separation of mixtures, and the various spectrographic methods for the examination of isolates—have become the eyes of the modern organic chemist in much the same way as the microscope has been to the biochemist. In no other field of chemistry have these techniques been more useful than in the study of essential oils and other fragrance materials. Some of these methods, which have replaced the complicated, time-consuming and uncertain methods based on chemical degradation,[1] have become popular only within the last ten years and are still so new that they have not been applied to the study of perfume and flavor materials. The following several examples have been chosen to demonstrate the gamut of these techniques as applied to the examination of known materials and also to new compounds.

The four primary alcohols geraniol, citronellol, nerol, and 3,7-dimethyl octanol-1 challenged the efforts of outstanding chemists for many years before their structures (Fig. 1) were established. The first example deals with the examination of a mixture of these four alcohols.

These alcohols are difficult to separate quantitatively by fractional distillation because of their similar boiling points. However, vapor phase chromatography (VPC) effects complete separation in a matter of minutes. It is true that proper conditions of gas flow, temperature, column packing, and other variables must be established before satisfactory results can be obtained, and this requires extended study and experience, but once these conditions are found, the results are easily reproducible. Fig. 2 shows the analytical separation of such a mixture on a conventional 10′ column packed with amine-treated polyethylene glycol monostearate on acid-washed Chromosorb (35/80 mesh) at a temperature of 180° C., inlet pressure of 10 psig, a cell current of 180 milliamps and a helium gas flow of 50 ml. per minute.

The areas of the peaks give the composition of the mixture with an absolute accuracy of ±0.6 per cent. The correlation of peak to component is most easily established by adding more of each component to

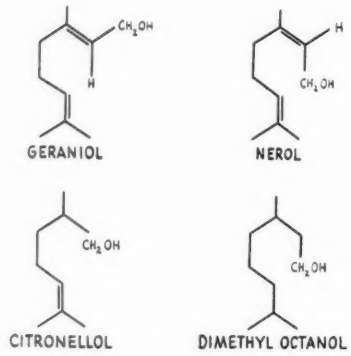

Figure 1. Structures of geraniol, nerol, citronellol and dimethyl octanol.

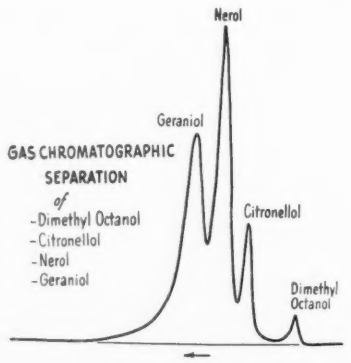

Figure 2. Gas chromatographic separation of a mixture of geraniol, citronellol, nerol, and dimethyl octanol using a conventional column.

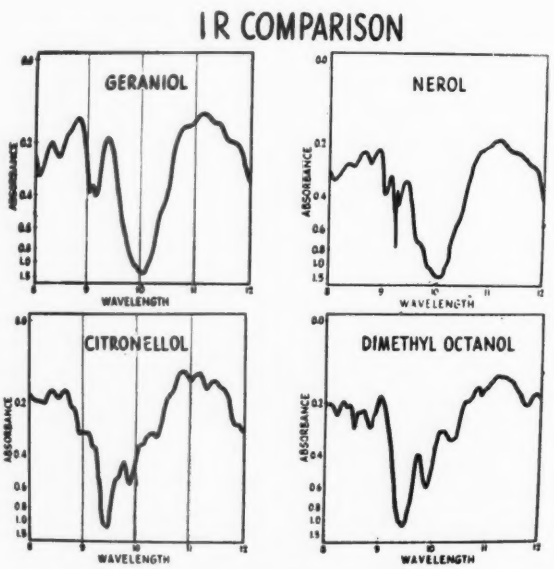

Figure 3. Infrared spectra of geraniol, nerol, citronellol, and dimethyl octanol in the 8-12 micron region, showing spectral differences.

*Reprinted from the Proceedings of the Scientific Section of the Toilet Goods Association, No. 32, 1959.

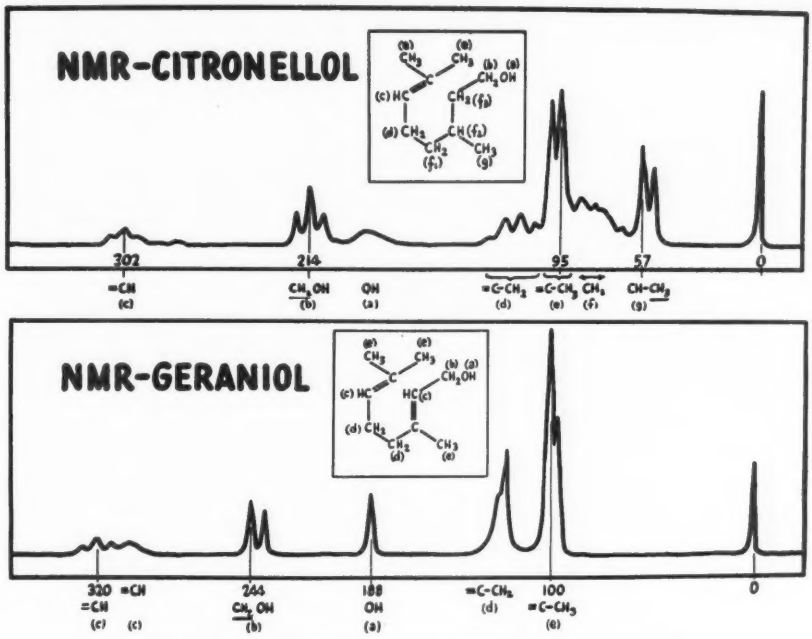

Figure 4. Nuclear magnetic resonance spectra—citronellol, geraniol.

the mixture to determine which peak increases. Greater certainty is achieved by trapping out each component as it is eluted, in an amount sufficient to prove its identity. For this the amount obtainable from the ¼ inch diameter analytical columns is not always sufficient. Large bore, so-called preparative, columns of ⅝ inch and ¾ inch diameter have been employed successfully to obtain as much as five milliliters of trapped component in substantially pure form from a mixture such as illustrated. With increase in column diameter, the problems of uniform packing and maintenance of constant conditions are multiplied, but with careful attention to all details the resolution on these larger columns will, in many cases, equal that obtained on the analytical instruments. In cases where packed columns do not have sufficient resolving power, the recently developed capillary columns may often be employed to effect much greater resolution. This will be discussed later.

A substantially pure compound, for example, one of the components of the above alcohol mixture, which has been isolated by trapping from a preparative VPC apparatus, is examined by any one or a combination of the various spectroanalytic techniques —ultraviolet, infrared, mass, and nuclear magnetic resonance. None of these techniques requires much sample—500 milligrams of trapped compound will usually serve for a complete examination. Study of minor components of mixtures is thus within the range of practicability.

Fig. 3 shows the infrared spectra of the four alco-

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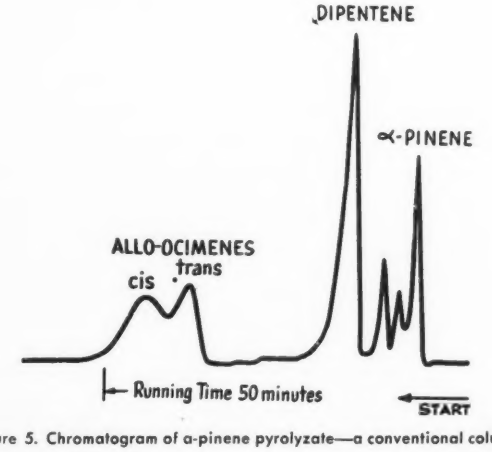

Figure 5. Chromatogram of a-pinene pyrolyzate—a conventional column.

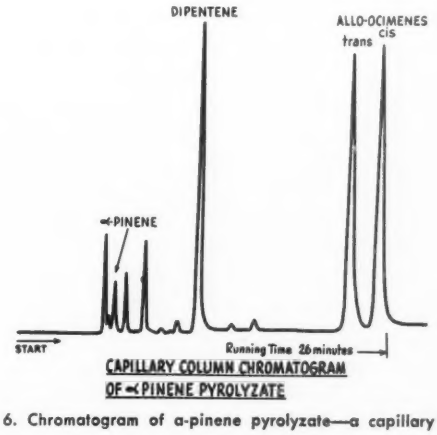

Figure 6. Chromatogram of a-pinene pyrolyzate—a capillary column.

ANOTHER KISSING DISEASE
Herpes Simplex

BY ARTHUR H. BRYAN, D. V. M.
JACKSONVILLE UNIVERSITY, FLA.

Herpes simplex, or Herpes labialis (also known as Herpes febrilis or facialis)—so-called fever blisters or cold sores—may be defined as an acute viral infection with a predilection for the labial mucous membrane. The disease is characterized by local eruptions in the form of individual or multiple vesicular lesions with slightly elevated inflammatory bases. The vesicles are filled with a clear seromucous fluid exudate. The definition may be restated as a mild dermotropic, acute, eruptive virus disease of the skin and mucous membrane characterized by vesicles containing serous fluid, with subsequent scab formations but no scars. Vesicles on the lips and nostrils (cold sores), on the genitalia, or associated with fevers (Herpes febrilis, fever sores) are most common. The vesicles usually appear within 24 to 48 hours, and last about 7 to 14 days. Herpetic infections have been reported following prolonged osculatory contact, local irritation, exposure to cold, heat, ultraviolet light, and other factors, dependent largely on the individual.

Virology

Herpes virus is filterable through Berkefeld V and N candles. It is about 150 mμ in size, and is thermolabile, for a temperature of 50° C. destroys it. The virus may be cultivated in tissue cultures and in the developing embryo. Tintranuclear inclusion bodies have been described in the lesions.

When the virus is inoculated into the scarified surface of a rabbit's cornea, a keratitis is produced. Virulent strains may become neurotropic, involving the central nervous system. A fatal encephalitis has been produced in rabbits, and the intracerebral injection of herpes virus into mice produces characteristic transmissible encephalitis (so-called brain fever).

Infection with Herpes simplex virus differs from most virus diseases in that the duration of immunity is uncertain or, at best, of short duration. Neutralization tests have demonstrated that the serum of persons recovering from local herpes lesions have neutralizing antibodies. Complement fixation antibodies also have been found as sero-diagnostic aids. Antibodies have been noted in the serum of persons who paradoxically develop herpes simplex, perhaps indicating a persistent latent infection.

Predisposing Factors

Men who work outdoors for long hours and are

exposed to the hot summer sun or to extreme cold for long periods, appear to be predisposed to fever blisters and cold sores. The lesions appear on the upper and lower labial mucous membrane and the adjacent epidermis or skin of the upper and lower lips. In addition to these climatic conditions as predisposing factors, cold sores and fever blisters are frequently—in fact all too frequently—associated with kissing, as a very obvious but usually pleasing mode of direct transmission. Here the virus may be transferred from lip to lip, if one or both contributing parties has an active or latent herpetic infection. The heavy pressure often concommitant with protracted osculation may so traumatize the ordinarily impervious, protective mucous membrane, that the Herpes simplex virus, if present, may invade the submucous tissues, and foment the pathology characteristic of the disease. Similar vesicles may also occur on the mucous membranes of the genitalia. Still another disease of allied virus origin is gingivostomatitis, which occurs in young children. Its mode of transmission is unknown.

Clinical Observations

Clinically and statistically, physicians, cosmetologists, and pharmacists note that women seldom suffer from herpetic lesions of the lips. This is undoubtedly due to the protective and possibly antiseptic action of the content of the casual lipstick in daily use by women. This hygienic fact is so well known, that manufacturers have developed lipsticks for men only. Male lipstick functions as a possible protective and antiviral device against these disfiguring and painful fever blisters and cold sores, sometimes provocatively but erroneously called "kissing ulcers."

Therapy and Prophylaxis

In spite of these male lipstick prophylactic measures, cold sores and fever blisters are still all too common and, to date, treatment has only been symptomatic, and, incidentally, none too effective. The painful lesions appear to run their course in spite of locally applied unguents, or solutions of antiseptic and antiviral agents such as antibiotics, sulfonamides, and other biotherapeutic or chemotherapeutic preparations. Furthermore, the initial viral infection may be complicated by those pesky secondary invaders, the staphylococci, resulting in further local tissue destruction, with local eruptions that may spread to the surrounding epidermal tissues.

Therapeutic Preparations

Up to the present, there appears to be no specific treatment for herpes simplex. Symptomatic relief with pharmaceutical preparations is being attempted, along with attempts at prophylactic measures. Among the well-known local applications used in prescriptions are compound tincture of benzoin or collodin; camomile lotion or phenolated calamine lotion; 2 per cent hydrocortisone lotion; cetyl pyridinium chloride in a 1:3000 solution; benzalkonium chloride in a 1:1000 solution; bacitracin ointment, 500 units per gram; Aureomycin ointment 3 per cent; and sulfonamides in ointments or unguents. In addition, applications of dusting powders and drying lotions such as Burow's solution have been tried therapeutically, to arrest the course of the disease.

Medicinal and nonmedicinal lipstick preparations have been tried as prophylactic measures to prevent these herpetic lesions especially in men. Women who use lipstick regularly encounter cold sores and fever blisters less frequently, despite prolonged osculation. In men, the reverse tends to be true, as they seldom use protective lip preparations. It is obvious then, that some new viricidal or chemo-therapeutic agents are needed to ameliorate, cure, or prevent Herpes simplex labial infections.

Requirements for a Therapeutic and Prophylactic Lipstick

Antiherpetic local preparations should (1) protect the labial mucous membranes during kissing or long over-exposure to the hot sun or to extreme cold; (2) dry or dehydrate; (3) possess antiseptic or antiviral properties; (4) soothe or serve as an analgesic in relieving pain; (5) heal, by promoting granulations tissue or cell repair; (6) have an astringent effect to reduce swelling and blisters; (8) be pleasant in odor and taste; (9) be heavy or waxy, so that they remain potent and adherent for some time on the sore lips; (10) act as a prophylactic in preventing recurrent, or latent, active infections; (11) be therapeutic in prompt cure or amelioration of the symptoms; and (12) be long lasting, both therapeutically and prophylactically.

Because Herpes simplex infections are mild and usually run a regular course, the physician is seldom called upon to treat cases, except when symptoms become severe or systemic. The druggist therefore may prescribe the therapy or palliative treatment for uncomplicated cases.

An effective medication against Herpes febrilis infections should meet the foregoing requirements.

Clinical experience seems to confirm that greasy preparations made with basic paraffin, lard, hydrous or anhydrous lanolin or petrolatum, are of doubtful value, irrespective of the therapeutic ingredients they may contain. In fact, such ointments appear to soften, or even assist in the spread of the infected areas, with the result that the etiological virus is not halted in its penetration of the surrounding tissues.

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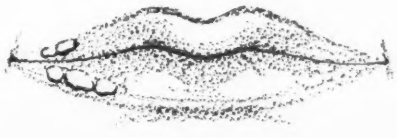


RIKER LABORATORIES, INC.

Riker Laboratories, Inc., the ethical pharmaceutical subsidiary of Rexall Drug and Chemical Company, is located on an 18-acre plot in Northridge, California, which provides for possible future expansion to more than twice the present floor area of 80,000 square feet. The layout provides flexibility for expansion in administrative, manufacturing, and research activity, flexibility in space utilization, and flexibility of services. Riker also operates four international subsidiaries in Canada, England, Union of South Africa, and Australia.

George L. Maison, M.D., president of the company, heads the administrative group, which includes J. W. Stutzman, M.D., Ph.D., vice-president and director of the research division, Alfred H. Ridges, vice-president and director of the division of sales and promotion, and Seymour H. Mann, vice-president and director of the manufacturing division. Research is coordinated by the director of laboratories, John E. Campion, Ph.D., and is subdivided into sections of medicinal chemistry, biological sciences, analytical and pharmaceutical chemistry, medicine, and patents, with a total staff of 73 in 1958.

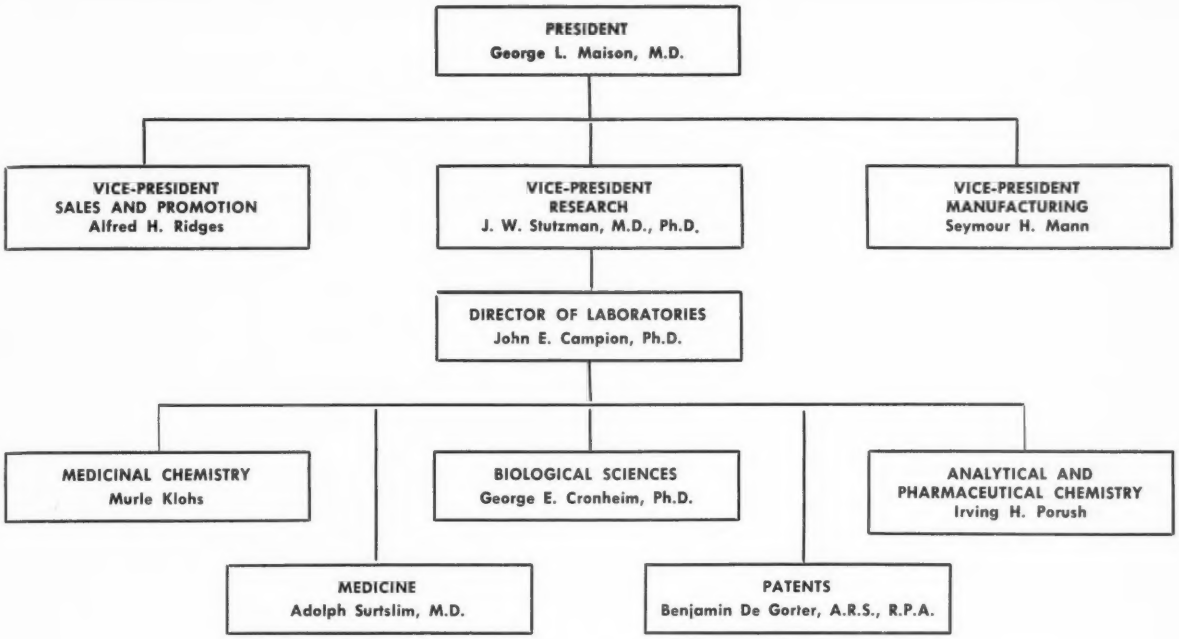
Medicinal chemistry, headed by Murle Klohs, is concerned with synthesis and isolation of chemicals for medicinal application, investigation of natural extracts, structure elucidation, and the development of patent information and data.

The section of biological sciences, including pharmacology, toxicology, physiology, and biochemistry, is led by George E. Cronheim, Ph.D. Duties of the section include determining the mechanism of drug action, absorption, and excretion, efficacy, and toxicity.

Analytical and pharmaceutical chemistry, under Irving H. Porush, develops dosage forms for drugs and analytical methods for determination and control, and also determines stability of products. Albert Surtshin, M.D., medical director, heads the medical section, which evaluates animal research and toxicity data and set up clinical studies leading to FDA acceptance and marketing.

The patent section, under Benjamin de Gorter, A.R.S., R.P.A., prosecutes patent applications, and provides patent information.

Major subdivisions of the manufacturing division are the pilot plant, for adapting laboratory processes to plant manufacturing, and testing process improvements on a smaller scale; the processing unit, an outdoor set of operations for drug extraction and chemical manufacture; the tableting and ampuling units; the aerosol unit; the packaging unit capable of filling and labeling 120 bottles containing 100 tablets per minute; order picking and shipping; and the power house. Staff members include W. Coleman, warehousing and shipping; R. Croad, aerosol; G. Gleason, maintenance; K. Gross, chemistry; L. Karch, scheduling; N. Lagoon, tableting; M. Margolies, pharmacy; T. Nitta, pilot plant; R. Popp, engineering; L. Tomalas, packaging; J. Van Ness, processing; R. Whitney, cost accounting. In the sales division, the sales manager, Charles Adams, correlates and integrates the work of the nine district managers; training is the function of Fred Goldthorpe; the advertising manager is Robert Service; Howard Houghtaling collates and summarizes reports and results; and export sales are supervised by Ramon Perez.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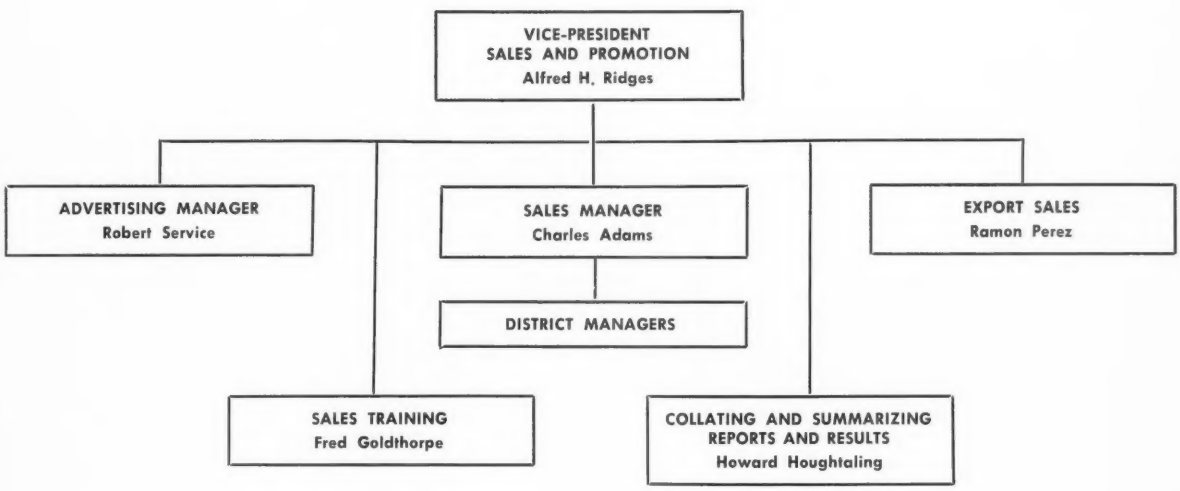
Irving H. Porush
MEDICINE
Adolph Surtslim, M.D.
PATENTS
Benjamin De Gorter, A.R.S., R.P.A.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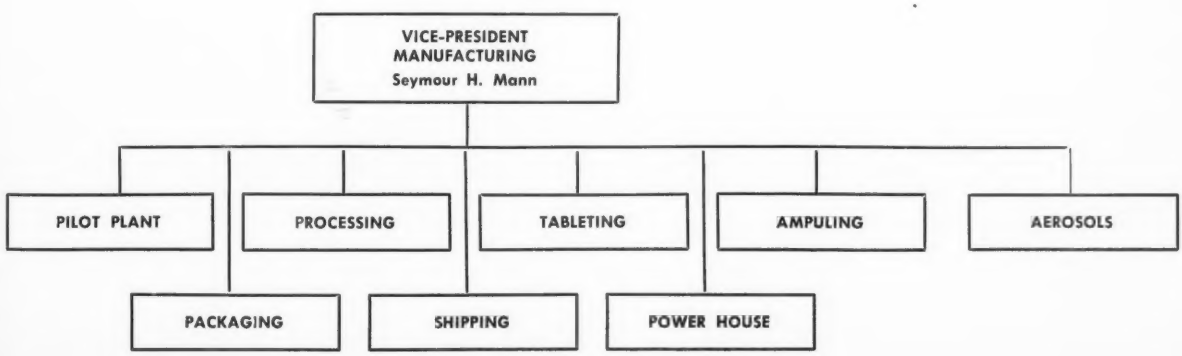
Howard Houghtaling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METHIONINE IN COSMETICS AND PHARMACEUTICALS*

BY H. J. PREBLUDA, Ph.D. AND IRWIN I. LUBOWE, M.D.†

It has been known for some time that—sulfur containing compounds play an important role in our biochemical processes of living systems. The year 1960 will mark the 150th anniversary of the discovery of the first amino acid, cystine, by Wollaston.[1] Little did Wollaston realize that his cystine contained sulfur. It should be noted that there was a time lag of almost one hundred years before the structure of cystine was fully established.[2, 3]

Methionine was not discovered until 1922.[4] Although its discovery can be considered relatively recent as compared to other sulfur amino acids, there has been an unusual amount of research to provide some background on the interrelationships of methionine with cysteine and cystine. The latter two amino acids are interconverted to one another in a reversible manner. We now know that, in higher animals, methionine can be incorporated into protein of biological systems and can play a role in the formation of cysteine and cystine, which are important amino acids in the make-up of skin and hair. Whereas methionine can be changed to cysteine and cystine in the human body, the reverse is not true. Cystine can function as a precursor of taurine for the synthesis of surface-active taurocholic acid of bile. Methionine is strictly indispensable and can fulfill the functions of cystine as well. Although cystine exerts a sparing action on methionine, it can show biochemical effects only when the methionine intake is not too severely restricted.

Methionine is a strong methylating agent and participates in the synthesis of many methylated compounds such as choline, creatine, and adrenalin. This amino acid, more than any other, enters into a great many metabolic pathways which either directly or indirectly control the rate of tissue catabolism and anabolism.

Commercial Synthesis

During the early 1940s, the U. S. Industrial Chemicals Company pioneered semi-commercial synthesis of the racemic mixture of DL-methionine. It has been shown that DL-methionine is an exception to the rule of most amino acids in that it can be used by human beings with equal biological efficiency as naturally occurring L-methionine on a weight for weight basis. The L-isomer of methionine tastes flat whereas the D-isomer has a sweet taste.[5] As a lipotropic agent, D-methionine can be as effective as L-methionine. Bacteria seem to prefer the natural form

*Reprinted from the Proceedings of the Scientific Section of The Toilet Goods Association No. 32, 1959.

†Dr. Prebluda is with U. S. Industrial Chemicals Company, New York, N. Y., and Dr. Lubowe is with the Metropolitan Hospital Center of New York Medical College, New York, N. Y.

of methionine to the D-form. However, there is evidence for the presence of DL-methionine in *L. arabinosus*.[6]

During the late 1940s synthetic methionine found ready use in lipotropic preparations formulated by the pharmaceutical industry. At that time, the animal feed industry started to use the sulfur amino acid product on a large tonnage basis. Whereas, in the early 1940s, the pharmaceutical grade of methionine sold for about a dollar a gram, it is presently available for considerably less than a cent a gram.

The large-scale commercial production of the synthetic racemic mixture of methionine helped accelerate the development of many new, unusual applications of this amino acid for pharmaceutical products.

Because of the great impact of the vitamin era on new product planning in the food and pharmaceutical industries, it should be kept in mind that the physiological dose of an essential amino acid like methionine is several hundred to one thousand times as great as some of the vitamins. This accounts for the use of food products as vehicles for the amino acid when doses of several grams have to be taken each day. It has been estimated that at least 20,000 tons of DL-methionine have been used in the last ten years to fortify animal feeds, food supplements, and for the manufacture of pharmaceutical products throughout the world.

Polyfunctional Properties

The purpose of this presentation is to summarize some of the newer developments pertaining to the use of methionine for cosmetics and pharmaceuticals.

A review on the various dermatological and pharmaceutical applications of this amino acid mentions that "it is doubtful there is any other material with such unusual diversity as methionine in its medical applications. The practitioner should be alerted and made aware of its variety of properties which are so important in understanding the pharmacodynamic disturbances of lipid, protein, sulfur and water metabolism."[7]

Another review[8] on the use of methionine in cosmetics mentions that furnishing a diet rich in methionine and poor in cystine brought about an increased formation of hair and its content of cystine.

Dr. M. X. Sullivan of Georgetown Medical School has found that increasing the methionine intake improves the strength of fingernails.[9] He found a correlation between the decreased sulfur amino acid content of fingernails and arthritic conditions. Studies have also shown a drop in the sulfur content of hair and nails of patients with cancerous cachexia.[10] Russian researchers have also confirmed this with male cancer patients.[11] Some mention should also be made of a report describing the feeding of hydrolyzed wool rich in sulfur amino acids to patients for hair treatment.[12] A hair-treating preparation consisting of equal weights of DL-methionine and serine has been patented.[13]

Topical Cutaneous Therapy. Lubowe[14] has been conducting clinical trials with methionine and other compounds in the topical treatment of pilo-sebaceous dermatitis and other cutaneous diseases, particularly acne, seborrheic dermatitis and capitis. He recently reported the results of an estrogenic amino acid preparation containing a methionine derivative in the treatment of acne and seborrheic capitis. The acne formulation is as follows:

Bentonite-iron oxide	2.00 gm.
Estradiol	0.32 gm.
Resorcin	2.00 gm.
N-acetyl DL-methionine	1.00 gm.
Colloidal sulphur	5.00 gm.
Propylene glycol	6.00 gm.
Foundation powder base q.s.ad.	100.00 gm.

Another topical preparation consisting of estrogenic hormone in combination with amino acids (methionine), a vasodilating substance, and an antiseptic has been used effectively on 80 per cent of the patients to alleviate seborrheic capitis and hair fall. The symptoms of itching, crusting, dandruff, and associated hair fall diminish with daily use of this scalp conditioner.

Wound Healing. There have been several favorable reports on the value of supplementary methionine on wound healing in protein depleted animals and humans. Localio[15] first showed that the defective healing of stubborn wounds could be restored to normal by simply adding methionine to the diet of clinical patients. Williamson[16] tagged methionine with radioactive sulfur (S^{35}) and confirmed the beneficial effect of methionine. His work showed a direct relationship between the increase in tensile

(Continued on page 847)

PHOTO COURTESY HELENA RUBINSTEIN

SCHERING'S QUALITY CONTROL

BY WILBUR S. FELKER, MANAGER OF QUALITY CONTROL, SCHERING CORPORATION

At a dedication ceremony on November 19, Francis C. Brown, president of Schering Corporation, officially opened the company's new $1.2 million Quality Control Center. Featured speakers on the occasion were George P. Larrick, Commissioner of the Food and Drug Administration, and Dr. Mason W. Gross, president of Rutgers University.

The Schering Quality Control Department was established in 1938 as a one-man testing program with the bulk of the testing done by outside laboratories. It quickly expanded into a number of locations in Bloomfield and Union, and is now centralized in the new building. Over 100,000 tests are made each year at a cost of more than half a million dollars. (See floor plan, page 764.)

The new center contains administrative offices and the two sections, analytical control and biological control. The facility at Union, N. J., is a two-story steel frame and cinder block structure set on piles, brick-faced and having three-quarter-inch fiberglass insulation on a steel roof deck. It is 222 feet, 6 inches long; 62 feet, 6 inches wide; 27 feet, 4 inches high; and encloses a floor area of 26,680 square feet. Now providing administrative offices, equipment, and services for a staff of 63, the building can accommodate 90. Three separate and distinct air-conditioning systems are provided for the sterile laboratory section, the toxicology section, and the analytical laboratories. The first has four different filters in the air-handling unit and ultra-violet lamps to assure a sterile air supply; the toxicology unit has a chiller and indoor cooling tower for nonstop operation and a constant temperature and air supply; and the analytical laboratories and offices have their own air-handling unit.

The analytical control laboratory is divided into four units with the group leaders at each corner. One side is a mirror image of the other, joined by a common work area where special hoods are located. Each analyst has all the facilities and equipment for standard tests; flanking both sides of the laboratory are equipment and reagent storage areas.

Three main sections of the laboratory handle raw material and intermediates; tablets, creams and syrups; and steroids, parenterals and other solutions and suspensions. In addition, the laboratory tests samples from all over the world for the International Division of the corporation. In 1958, the analytical laboratory performed approximately 100,000 tests on over 20,000 samples. Testing in connection with stability determination and product development is done here.

The methods improvement laboratory adjoins the analytical laboratory, and is concerned with the de-

Sterile testing area has sterile air supply, requires sterile clothing.

In analytical control laboratory each analyst has standard equipment.

Raw materials sampling, an essential first step for quality control.

velopment and improvement of assay methods. All special testing is carried on here. Each of the two areas comprising this laboratory is divided into modules completely individualized for four chemists. The rooms are designed so that chemists can work independently or as a team.

The instrument room houses the precision instruments used for the analysis and identification of raw materials and final compounds. Instruments used here include colorimeters, polarographs, a recording spectrophotometer, vapor fractometers, and an infrared spectrophotometer. The area has sufficient ventilation for the use of flame spectrophotometry, and features controlled temperature and humidity.

Next to the instrument room is the dark room for analyses that require light conditioning, such as polarimetry and fluorescence studies.

Adjoining the analytical laboratory are complete facilities for the washing and storage of glassware and equipment. Also included are separate administrative office space for the laboratory, and locker rooms for men and women employees. The reagent room, for making and storing standard solutions and special reagents for general laboratory use, features spark-proof floors and telephone, vapor-proof lighting, and special ventilation.

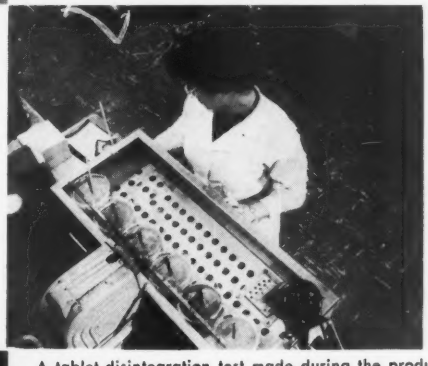
Analysis of raw materials, here determination of capillary melting point.

The biological control section is the second major subdivision of the new quality control center. Entry to this section is gained through the glassware unit where all glassware is cleaned and sterilized. In the adjoining media laboratory, all media are prepared for use and dispensed into flasks and culture tubes. At one end of this room the media are autoclaved and then removed to the adjoining sterile media storage area. Plating, culturing, and identification of various organisms take place in the bacteriology laboratory. Here special experimental work is performed, including serial dilution studies, mold growth, preservative activity, and routine water-control tests necessary in the manufacture of sterile products. Incubators to work at all temperatures are also located here.

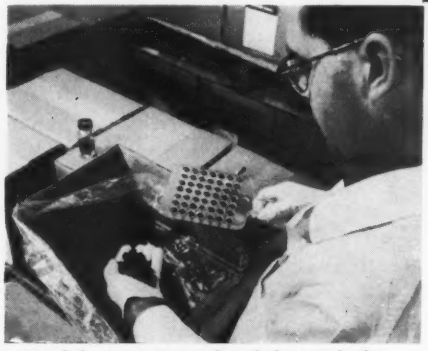
The microbiological assay section performs assays for the antibiotics penicillin, streptomycin, neomycin, gramicidin, and griseofulvin. This room is equipped with incubators duplicating the facilities found in the bacteriology laboratory. Veterinary preparations containing antibiotics are also tested here.

Beyond this point is the sterile testing area. Each section must be completely closed off before one enters the next one, and sterile clothing is required. The four-stage air-conditioning unit for this area includes: rough filter, electronic precipitator, roll-up blanket filter, and absolute filters, along with ultraviolet lamps in the ducts to insure a sterile air supply.

All sterility testing for the company is carried on here. Two inoculation booths isolate the operators. Three walk-in incubators with adjustable temperature provide for bacteria and mold-growth tests at any testing temperature.



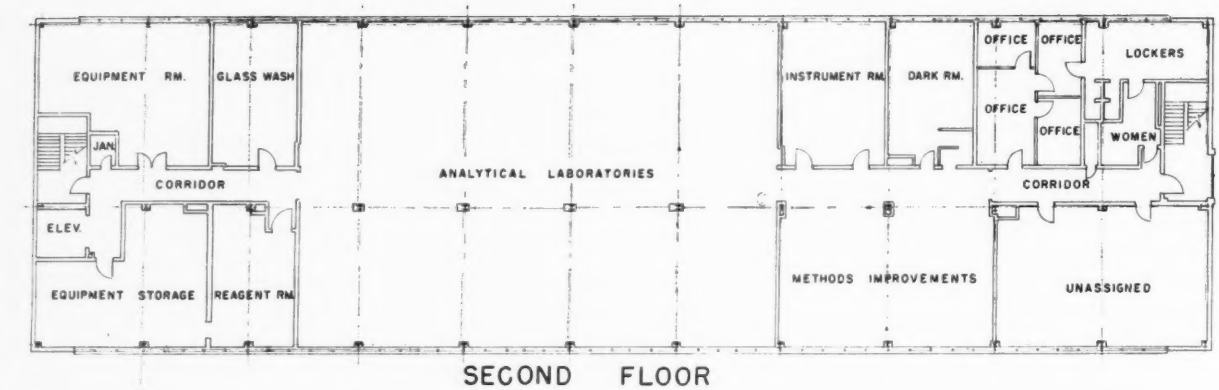
A tablet-disintegration test made during the production of the product.



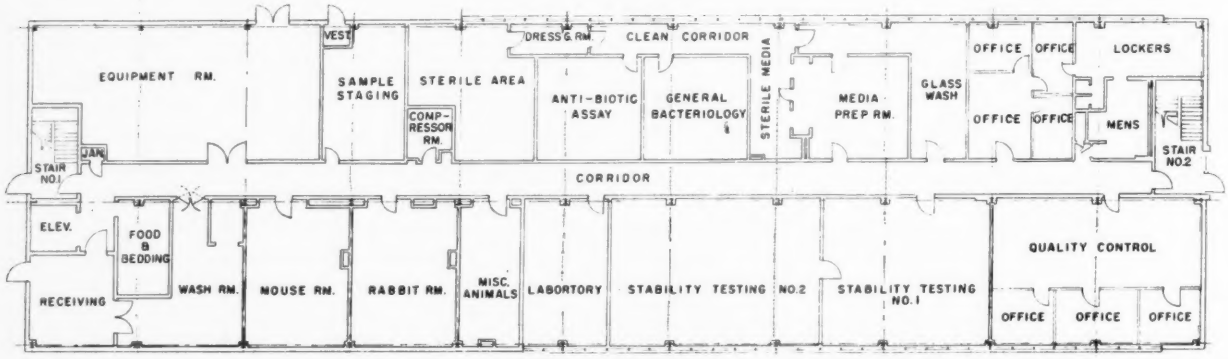
Bulk tablet inspection, one of the many steps taken during production.

On the opposite side of the building is the toxicology control laboratory, an important unit of the biological control section. This section consists of a toxicology laboratory and three animal rooms with fully equipped washing and sterilizing rooms for animal cages. Controlled animal assays and studies requiring special techniques are carried on here.

Eye-irritation tests for ophthalmic preparations and pyrogen testing for parenterals take place in the rabbit room. Routine irritation tests on ophthalmics, creams, ointments, and areosols, as well as



SECOND FLOOR



FIRST FLOOR

safety toxicity tests on all products are performed here.

Administrative offices contain the master specifications file for the entire corporation. This file records all details of manufacturing and control on each product, for record and for future reference. Only after all data have been assembled in the quality control office and evaluated, is a batch certified for release.

In this office, quality control personnel write and maintain control sections of New Drug Applications, establish specifications for raw materials and finished drugs, devise sampling schedules, and set up specifications for government contracts and for subcontractors. Also handled are evaluations of clinical material requisitions, audits and tests for the International Division, and investigations for the Law Department and Product Service Department.

Other important areas of quality control include the staging area, where all samples enter the building and are registered and prepared for distribution to appropriate testing laboratories; the stability storage area where refrigerators and incubators determine or confirm shelf life of all Schering products for testing periods as long as three years.

Since even slight variations from the original amounts and qualities of the drug prescribed might have serious consequences, quality control is of paramount importance in this industry. Quality control is specifically the effort to detect deviations in the manufactured product from original specifications, and to prevent and to correct these deviations before the product reaches the consumer. Continuous inspection and analysis of raw materials, packaging supplies, and finished packages, along with rigorous control of manufacturing processes and packaging are essential.

The final consumer package is the culmination of research origin, activity and safety determinations in the biological sciences departments, final approval resulting from clinical investigation, compounding of desirable dosage forms, development of effective manufacturing procedures, and selection and assembly of packaging components. These are integrated to provide specifications—detailed descriptions and definitions in words and numbers, expressing all the qualities of the product. Specification subdivisions include purity specifications for raw materials, finishing specifications for sales-package components, procedure specifications for work and equipment layout, and specifications for testing methods, topped by the master product formula specification.

Segregation, another element of quality control, is, essentially, organized good housekeeping. It involves such things as the detention area, where incoming and outgoing stocks are held for inspection and analysis; protected storage facilities for narcotics and

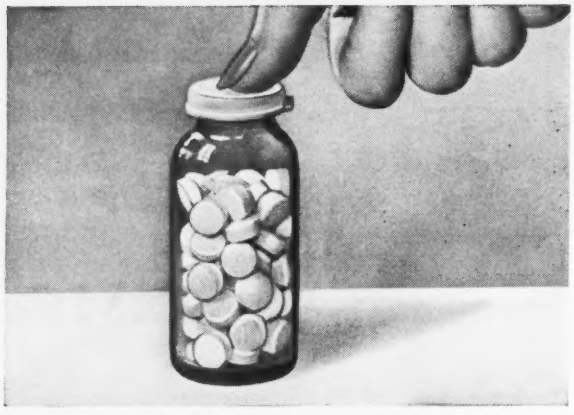
(*Continued on page 836*)

Packaging and Selling

New design for Ciba Pharmaceutical

Products, Inc., for its entire line of ethical pharmaceuticals, the color scheme a basic buff, combined with olive for single products, with orange for combination products, with purple for special forms (e.g. pediatric), with almond for differences in drugs in the same line. The design as well as the condensed Roman type face was created by Ciba's design section.

Off with ease



. . . closed tight quickly

The new Safety Cap keeps medications safe from children's hands . . . yet adults remove it easily

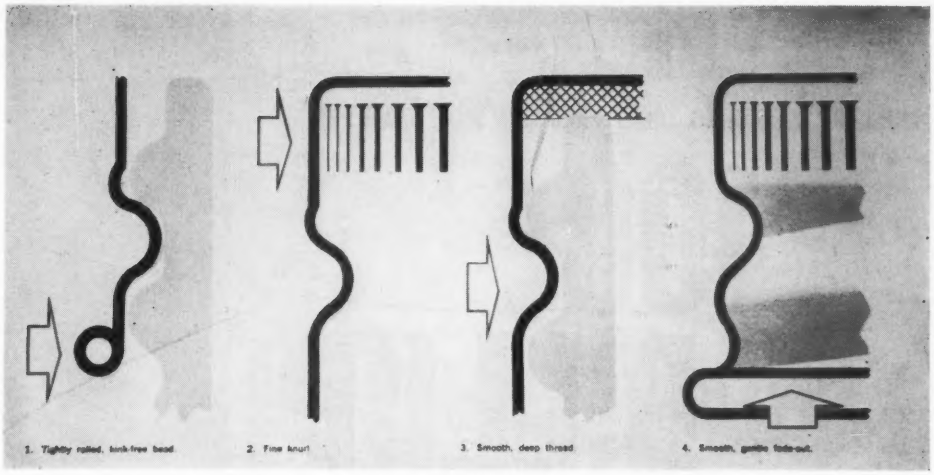
Owens-Illinois Snap-Caps
provide a perfect seal for dry products

Owens-Illinois plastic Snap-Caps offer use-convenience and tight, durable protection for dry products at all times. Off and on with a flick of the fingers, these tight-sealing closures stay clean and secure, no matter how many times they are handled.

The Safety Cap is another development from Owens-Illinois. It offers the advantages of Snap-Caps in ease of operation, yet it is difficult for little children to remove . . . keeps medications away from inquisitive hands. For complete information about Snap-Caps as the ideal closure for your package, call your nearest O-I office, or write to Owens-Illinois, Toledo 1, Ohio.

PRESSED PLASTICS
AN (O) PRODUCT

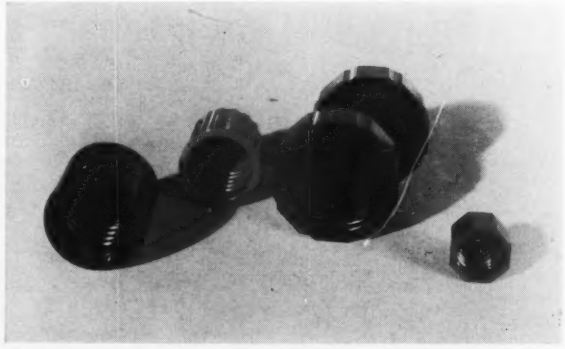
OWENS-ILLINOIS
GENERAL OFFICES · TOLEDO 1, OHIO



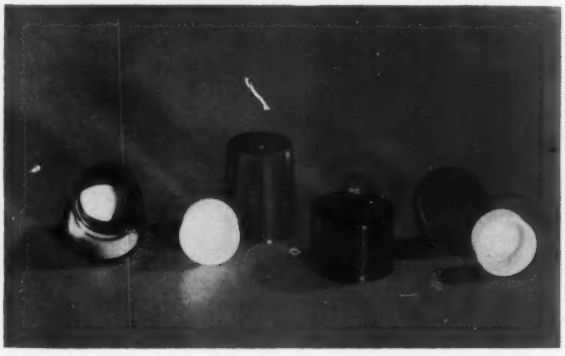
Features of the improved metal cap assist in easy starting of the cap on bottles on high-speed capping lines. Metal caps are functional, but lack the design possibilities and attractiveness of molded caps.

CLOSURES TODAY AND TOMORROW*

BY E. C. EMANUEL
ARMSTRONG CORK COMPANY



Originally, almost straight side-wall shapes predominated in molded caps. Embossing was readily accomplished. Note their heavy weight.



Thin-walled, lightweight closures, made possible by closer control of the tolerance of the glass finish, cannot withstand high-speed capping.

*Presented at the 21st Annual National Packaging Forum of the Packaging Institute, November 1959.

Metal Caps

With the trend away from the use of natural corks, which started in 1926, tin and aluminum screw caps either plain or lithographed came into general use —first for dry products such as pills, tablets, or capsules, and later for liquid products. The first closures were rather crude by today's standards, but through the years there has been steady improvement in the metal and in the use of synthetic resins in the varnishes and lacquers for internal and external protective coatings to reduce corrosion.

More recently, major improvements have been made in narrow-mouth metal caps wherein a tighter rolling of the bead, produced by a new technique, has strengthened the caps, reducing bending; a better thread design has been developed; and the knurl has been improved. These changes have produced metal closures better suited to perform in the high-speed capping lines without jamming or distortion.

Advances also have been made in tinplate, especially in annealing and temper, and newer aluminum alloys with improved properties are available. Metal caps have their place as closures, for they are functional, and will be used to seal containers for many years to come.

Molded Caps

In 1926, a new material, bakelite—a thermosetting molding compound made from a phenol-formaldehyde resin—was first used for screw caps. The molded cap became practical when glass manufac-

THE BEST REASON TO TRUST PRECISION WITH YOUR PRODUCT

*100 BILLION SUCCESSES WITH THIS VALVE

PERFORMANCE-PROVEN ON EVERY TYPE OF PRESSURIZED PRODUCT

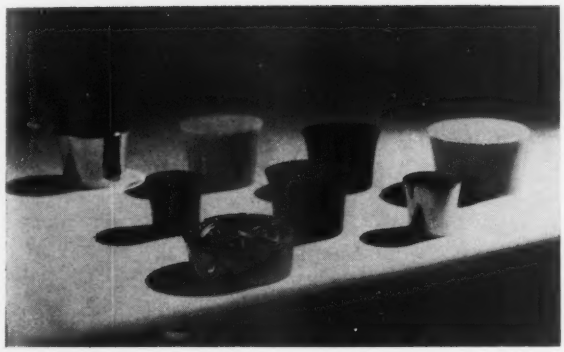
On October 18, 1959 at 10:25 in the morning, Precision Valve Corporation produced its one billionth aerosol valve. Ten years of research, study and experience went into its creation and in those same ten years, the aerosol package came of age.

Today, almost any product that can be poured or powdered can be dispensed in an aerosol . . . always dispensed with greater ease and more convenience, usually at less cost.

Precision Valve Corporation's Research Department will be happy to help you build a better package for your product with the valve of proven quality.

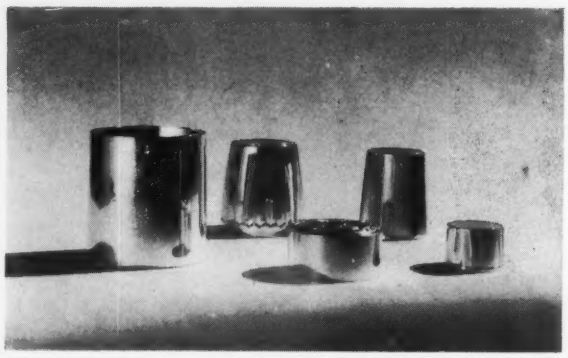
PRECISION VALVE CORPORATION
700 NEPPERHAN AVE., YONKERS, N. Y. • ZURICH

** Calculated on the basis of about 100 actuations per aerosol . . . from the 56 uses of an air sanitizer through the 198 times actuated tooth paste container, not including foreign production.*



Reversed, tapered molded caps, a recent innovation providing the charm and color variety desired especially for cosmetic closures.

Designs can be economically made in closure side walls by means of the electro-formed process for cavities from which caps are molded.



Simulated gold or silver finishes applied to thermosetting or thermoplastic closures. Recent varnish improvement gives them more resistance.

turers produced screw-finished containers within reasonable tolerance limits, so that the cap would fit the containers. Phenol-formaldehyde resin closures are available only in dark colors. It is interesting that, in the early days, 24 mm molded caps sold for $25 net/M, as compared to an average price today of about $5.50 net/M.

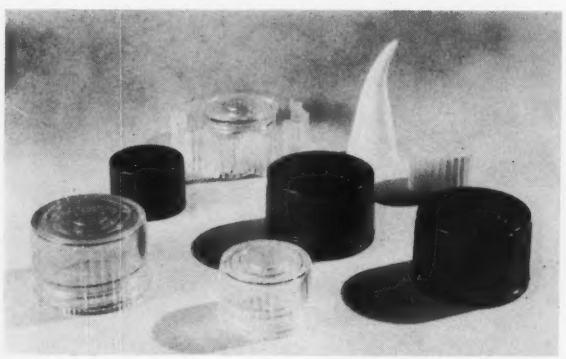
In about 1932, another thermosetting molding material based on a urea-formaldehyde resin became available. This light-colored resin is used to produce brightly colored caps from white to pastel shades, or for dark colors.

Both the phenol-formaldehyde and the urea-formaldehyde thermosetting molding materials are currently the materials from which the majority of molded screw caps are produced. In the intervening years, the powders have been steadily improved, are more unifrom from batch to batch, cure faster, are free of taste and odor, and give uniform performance.

Molded closures are attractive in appearance, have a smooth, bright surface, do not show the threads, have no bead, and can be made in limitless shapes or designs.

The first closures molded from the thermosetting materials were heavy-walled and slow in curing. They had very high strength. Part of the reason for the heavy structure of the wall was to develop strength to prevent breakage on the glass, which, while made within specifications, varied considerably. Through the years the tolerance of the glass finish has been brought under closer control, making lightweight caps possible. There was a trend from the heavy-walled caps to very thin-walled (eggshell) closures. These worked reasonably well on slow capping lines. Capping speeds have increased, however, and these thin-walled caps do not have sufficient strength to withstand the suddenly applied capping pressures; consequently, there is now a tendency to "beef up" the wall thickness, that is, to increase the weight of the closures to accommodate the high-speed capping lines. The closures have been

(*Continued on page 837*)



Thermoplastic caps. For each specific type, the molding cycle, molding temperature, and molding temperature must be worked out, tested.

Attractive caps are made from assembled, molded parts. This example of completed closure and pour-out shows the parts before assembly.

GLASS STIMULATES SALES
The graceful contours and pleasing proportions of our new 443 stock bottle make it an outstanding container for your finest products. With an attractive fired-on label it makes a cosmetic package of unquestioned beauty.
443
Toiletries
CARR-LOWREY GLASS CO.
Designers and manufacturers of fine glass containers
Factory and Main Office: BALTIMORE 3, MD. • New York Office: 415 MADISON AVE. • Chicago Office: 1572 MERCHANDISE MART

Packaging and Selling

How many people in sales and advertising are underestimating the power of the advertising dollar to produce sales?

Here's what a local advertising agency on the Pacific Coast was recently quoted as saying: "Clients from the East are constantly underestimating the amount of money that must be spent here to get any type of saturation. We recently had a client's executive come out and give us a rediculously low figure of $100,000 to introduce a new product.

"I did not protest. I just put him into a car and drove him around little old L. A. for a day. When he realized the great degree of decentralization of population here, he got on the phone to New York and increased the budget fivefold."

Another coast agency man had this to say: "We are also faced with a consumer population that is always new, as a result of the hordes of people settling here.

"This means that they are not familiar with even our established brands, and we can never promote a type of institutional brand-consciousness."

These are opinions of two leading local advertising agencies for the specific problem of the Pacific Coast. We do not see that these problems vary in the slightest from any other section of the United States. Also, wherever you go, you find the same degree of decentralization of population, the same degree of bursting population growth, and the same degree of movement of population.

For this reason, if we determine the amount of money needed in the national United States market using the sums apparently needed for the Pacific Coast as a fractional base, we can see how few of the advertisers in any industry are attaining any degree of effective pre-selling of their brands.

"The curve of business has a very definite effect on the curve of the art and the look of advertising." This is what Mr. Morris Rosenblum, creative advertising administrator of Macy's, said in a recent talk.

Advertising changes with the economic climate. According to Mr. Rosenblum, in the sellers' market preceding the depression of 1929 advertising tended to become understated and idealized, making little effort to sell because little was needed.

On the other hand, after the crash it became necessary to use realistic illustrations and bold, black type.

Although business is booming today, he stated, inflation, narrow profit margins, and increased expenses make it necessary "to get every dollar's worth for every advertising dollar spent."

In newspaper advertising, "the most important medium," this can be achieved through what Mr. Rosenblum calls "graphic drama." This is the process of stop, look, and read. An ad has four seconds to stop the reader, said Mr. Rosenblum, because "that's the time it takes to turn a newspaper page."

Some of the big people in the food business seem to be ready to give up the fight on private label. Whether this is ominous may be judged from the comment of an executive who is now ready to start a $2 million advertising campaign for a specialty food product.

"Dealing with one of the prime aspects of a national promotion for such a product," he said, "we recognize the problem of private labels, but it is our feeling that combatting this would be financially impossible.

"Our experience has been that when a chain goes into private label they also keep at least one national or regionally advertised product in the freezer aside from their own. We want to make certain we are that brand."

Note again that this is a manufacturer spending $2 million for this product. We wonder how far in this direction this kind of thinking has gone in the food industry, and where it could be leading.

Investors and speculators in this country have placed the leading drug companies in the front rank of growth companies. So far as the last ten years go, this judgment has been proved more than sound; the lucky people who put some money in any one of the leading drug company stocks can now lean back with a satisfied feeling.

And yet, pharmaceutical profits are far from consistent so far as any one company is concerned.

In an editorial in the Cyanamid News, we came across a few provocative figures and remarks that show just how hard it is to pick a growth leader in this field and just how uncertain it is to stay with any one of these leaders for growth.

"According to the editorial, few miracle drugs survive as leaders for more than five years. Pharmaceutical manufacturers can only protect their future by plowing back the profits they make during those years into research to pace their competition.

"Estimates of the percentage of profitable drugs vary, but, conservatively speaking, a pharmaceutical company has less than a 50-50 chance of merely recovering its investment.

"Pharmaceutical profits, therefore, are hard to forecast. No company seems to have a consistent

Ucon brand propellants put action in products

UNION CARBIDE
Ucon
HRAND

Why don't you discover Ucon Propellant service, too?

UNION CARBIDE CHEMICALS COMPANY
Division of Union Carbide Corporation
30 East 42nd Street, New York 17, N. Y.

Ucon and Union Carbide are registered trade marks of Union Carbide Corporation

record of high earnings. The best years of the most successful pharmaceutical companies have earned them twice as much income as their worst. Among 12 important pharmaceutical enterprises—including the six leading antibiotic producers—Cyanamid has ranked all the way from second to last in different years on pharmaceutical sales; Pfizer has ranked from first to last; Parke-Davis from first to seventh.

"No leader has remained a leader long."

Some day this will be added to the archives of the cosmetic industry—an aerosol product, an oriental perfume called "Lady Chatterley's Instant Sexx."

As might be expected, the use by farm people of cosmetics, toiletries, and drugs averages up to nearly that of urban dwellers. *The Progressive Farmer*, an old, established southern farm magazine, which covers the belt of southern states, has just issued a market survey showing the brands and the percentage of southern rural families that uses each of these brands.

As an indication of how southern family consumption would compare to over-all U. S. consumption, the following percentages are revealing:

PERCENTAGE OF ALL FAMILIES USING	
Lipstick	78.1
Perfume and cologne	67.7
Bath or talcum powder	72.3
Face cream	61.6
Electric shavers	30.1
Deodorants	82.1
Toothpaste	90.1
Vitamins	47.1
Cough drops	60.8
Laxatives	74.5

"The Coming Battle with the Giant Retailers' Advertised Brands" is a new, complete study by E. B. Weiss, director of merchandising at Doyle, Dane, Bernbach, Inc., New York, Chicago, and Los Angeles advertising agency.

Two central ideas are developed in this study, namely, that, in the coming battle of the brands, there are two principal antagonists, the large manufacturer promoting advertised brands, and the giant retailer and giant retail groups promoting their own controlled and advertised brands.

The conclusion is that the unknown brand or the small brand is on the way to being really squeezed.

Of course, this thought is not new. The business press has been filled for two or three years now with the problems arising from the enormous growth of retailers' private brands, particularly in the food field. However, this study is comprehensive and provocative.

It might be pointed out that at least some major supermarkets today are reducing the choice and variety of products offered the consumer. Instead of a considerable number of brands, one is apt to find a store's private label prominently featured, alone with a choice of one or two of the top nationally advertised products.

What this trend means for many consumers is a lack of reasonable choice for a variety of flavors, kinds, sizes, or what-have-you and, sadly but very definitely, a substantial lack of choice for true quality.

One of tragic aspect of this battle of the giants may be that, simply because it is a battle among the giants of mass produced, advertised, standardization, there may be a real and substantial decline in true quality in many products.

The Ford Motor Company has decided to hang the funeral crepe on the Edsel automobile, marking the end of one of the most forceful and dramatic presentations of a new automobile.

As a matter of fact, the final passing of the Edsel car is an epic that should be written up in detail by a marketing man.

Here was a leading manufacturer with a name universally known and respected by the public, with a powerful retail dealer organization, with plenty of capital, with merchandising brains, and with a top national advertising agency selected after detailed interviews for over a year among 40 or 50 agencies, producing a new product with showmanship and drama that almost universally caught the public eye.

What in the name of all the geniuses in advertising and marketing could have happened?

Perhaps it is very simple.

As the book publishers once learned from a $100,000 marketing investigation they sponsored to find out what was wrong with their industry: Do not try to sell something the public does not really want. There is not enough money in the world for selling and advertising that could make the public buy something it does not want.

This really seems to be an epic example of a profoundly simple thought.

The Grand Central Station in New York will soon be completely equipped with brand new fancy lockers. The most interesting thing about these lockers, from our viewpoint, is that they will offer the first experiment in deodorization or perfuming. Each time the locker is opened a gadget will squirt a "fresh, outdoorsy aroma" into the locker.

Such terms as "federal," and "government," when used in advertising, may be considered as misleading the public and may be in for review by the Federal Trade Commission. This is a report based upon a recent examination.

Lord love us if we haven't got a new method of advertising! A company called Point-of-Impact, Inc., hopes to install in supermarkets floor tiles each containing a message from a national advertiser.

What will happen to shelf impact or impulse sales when everyone walks around with his eyes glued to the floor remains to be seen.

In our limited experience, the people who try to save money in bringing out new trademarks by avoiding either a full trademark search or going to a good trademark lawyer, very often end up in trouble.

We say this with feeling because, as publisher of the *Trade Mark Record* and of its three ensuing supplements, we are constantly meeting people of this kind.

Just recently a new cosmetic manufacturer came to this office with a big burden of grief and an inclination to blame us for his troubles. He is putting a new cosmetic on the market and has come up with an extremely interesting word to use as the trade name.

After carefully examining the original *Trade Mark Record* and all its editions, he arrived at the conclusion that the mark was not registered and so, immediately proceeded to complete his package, have his labels made, prepare circulars and advertising and show samples to a number of retailers.

At this time, after he had spent about $10,000 and committed himself seriously in a number of directions with good stores, he discovered that one of the big manufacturers had a product which is for sale in only two stores, but which has this identical trademark registered for the product.

It turns out that this name was listed in the supplement of our Record, but for some reason, not in exact alphabetical order, that is, in accordance with the first three letters of the word and, for that reason, it was missed.

The truth is that even if this trademark had not been listed in our Record or its supplements, this man had no right to assume that the word was free for his use and that he could proceed without further expense. Unfortunately, this industry has literally thousands of unregistered marks, many of which have secured position by operating in a very local way or, to be frank, marks which are registered but which we have happened to miss in all our careful search to keep these books in apple-pie order.

So, let the warning be on the record; don't just assume that these books will always save you any further labor or the fee for a good trademark attorney. If you intend to spend real money on a trademark, do a thorough job of research—which usually means a good trademark attorney.

A recent research among 300 housewives in five big supermarkets came up with the fact that 41 per cent of the things bought at the time of the survey were impulse purchases.

There is nothing startling or staggering about this conclusion. In fact, we wonder why anybody bothered to report it.

The impulse purchase is something that has certainly been given the maximum push-treatment in advertising circles during the last several years. The only thing that surveyors forget to report is whether the women would have spent any more money than they ordinarily would have spent in these stores at this particular time if there had been no such thing as an impulse purchase.

A purchase may be unplanned but that does not mean at all that the spending of that particular amout of money was unplanned. From the viewpoint of any one manufacturer, there is an essential element here indicating the need for the best possible display at the point of sale, but, from the viewpoint of the retailer, it might not make anywhere as near the difference that the hullabaloo for impulse sales might indicate.

The American Management Association has just completed a very interesting study on product planning. It was initiated because of the findings that top level management is devoting more and more time to the planning of new products.

The outstanding discovery in this survey was that the best ideas for new products come from salesmen.

Salesmen and sales reports are considered the best sources of product ideas, the study found. The next most fruitful source is that of research and engineering staffs. Finally, came suggestions from customers, as well as inquiries and complaints.

Among the companies interviewed, the majority reported that they were looking "for products that embody more and better features to build product uniqueness and identity."

The next largest group were looking for products "easier-to-use and for products to complete their lines."

Only a very few companies said that they were seeking more glamorous, appetizing or luxurious products.

Next year in Chicago, the first automatic merchandising all-vending-machine operated grocery store will be opened.

Perhaps this is a new step in the so-called retail revolution which will give us business editors a chance to fill up a lot of white space next year.

While the national average for the sale of health and beauty products in grocery stores is 2.3 per cent of total sales, various research has found that this can vary substantially in bigger stores.

In a recent check of actual sales for this department in 23 selected supermarkets, it was found that the percentage of total sales in this category ran from 1.16 per cent to an excellent 3.24 per cent.

The top store doing 3.24 per cent of total sales for the health and beauty department was found to produce more than 6 per cent of the store's gross profit in the same department.

It was found that for best results this department

should be given a minimum of 4 lineal feet for each 100 lineal feet of display space devoted to just groceries.

John Schwegmann, Jr., in New Orleans, has already made his reputation as a very tough fighter against price-maintenance authorities.

Now, in addition, an editorial advertisement he recently ran in newspapers is certainly something of a poser for price-maintenance authorities in this country of free and independent enterprises where competition is supposed to reduce costs and distribution is supposed to be an admired achievement.

Here's what the ad said in the headline.

"I Am Accused.

"A criminal charge has been filed against me. I had to post an appearance bond and my name is now on the criminal blotter. What am I charged with? What did I do? I am charged with violating the law by selling milk too cheap. . . . I am being forced by law to charge more . . . otherwise I subject myself to jail. Is it a crime to provide an extra glass of milk to families in our city? Reducing the cost of a glass of milk a few pennies might be the difference between sufficient and insufficient milk requirements for many of our children. . . . City health authorities should not intimidate those who fight for lower prices—these authorities should restrict themselves to health problems. . . ."

According to a leading research corporation, the chief characteristic of the American market is the "concept of change." The American market is in constant flux in the way people travel, change jobs, change restaurants, change their economic status, their education status, and in just about everything else they do.

According to this group, if you want to appraise the American market for a new or old product, keep constantly in mind this factor of continual change.

We have just received an intriguing new container from the Combinette Container Co. of 10 Seventh St., San Francisco 3, Calif. This is described as an "ideal shipping container and ideal to keep children away from dangerous modern medicines, pills, etc." Actually, it is a plastic vial with a large transparent plastic jar. The cap is a plastic combination of three revolving disks which set a combination number so that the cap can be lifted off the jar. The triple combination number for each jar is on a removable label on each jar.

In addition to a very interesting package for the medicine cabinet, which is certainly beyond the ability for tampering by children, the container makes an interesting novelty container with many other possible uses.

Cosmetics and toiletries are among the biggest volume users of national and regional spot television. During the second quarter of this year this group spent $13,349,000 in spot television. This is broken down as follows: cosmetics, $2,854,000; deodorants, $2,058,000; depilatories, $43,000; hair tonics and shampoos, $2,904,000; hand and face creams, lotions, $1,138,000; home permanents and coloring, $1,684,000; perfumes, toilet waters, etc., $229,000; and shaving creams, lotions, etc., $343,000.

The National Canners Association is doing something about a problem harassing every association and every manufacturer. That is, the problem of out-of-stock in a retail store.

This association has just completed a 12-week period study in the twelve supermarkets of the American Stores Company in the Philadelphia-New Jersey area. According to this study, "Despite the fact that these stores are among the most efficient in the country —that they have the advantage of a highly developed ordering system and rapid deliveries from a modern warehouse which services them—the survey revealed that an average of 3.2 per cent, or, about 23 of the 708 canned food items stocked were found to be out-of-stock on the shelf each day in each supermarket." As might be expected, "Many of the highest volume products suffered from the most serious out-of-stock conditions."

It will be a lot easier, in the future, for a man to get a tan according to the advertising of a new product called Man Tan, which is described as "a skin tanning after shave lotion with Vitamin D." The product is being put out by the Drug Research Corporation and is being market tested in a western state.

Marketing in the United States has probably reached the highest peak of intensity and development of any country in the world. Certainly we spend more money for advertising, and undoubtedly more money for selling. Here is an interesting comparison taken from *France Actuelle*. "Of all the French at work, 10 per cent are engaged in selling, compared to 17.8 per cent in the United States."

According to the English magazine *Scope*, an intense radiation plant now being designed by the Atomic Energy Authority to be built at the Wantage Radiation Laboratories can be used for the sterilization of medical equipment and the disinfection of packaged products. According to the magazine, "For example, the medical packs carried by aircraft can easily be sterilized with this equipment. Medical packs can be packaged in polyethylene bags and then sterilized by irradiation from the plant. They will then remain sterile until the pack is opened."

Packaged or canned foods can easily be disinfested by this system of intense radiation, but at present it affects the taste. It is emphasized that goods subjected to this radiation do not themselves become radioactive.

Aerosol packaging captures 51% of the $73,900,000 cologne market

If your product can be brushed, poured, sprayed or squeezed, this profitable new packaging idea can generate sales for you, too!

Sales of aerosol-packaged colognes reached $37,600,000 in 1958—51% of the $73,900,000 total spent on colognes—and they're still increasing at a rate of over 20% a year.

The reasons for this success are simple. Aerosols deliver the product in a completely new form that's easier, more effective and often more economical to use. If your product can be brushed, poured, sprayed or squeezed, you stand a good chance to add new sales appeal—create vast, new markets—if you package it in an aerosol.

It is not necessary to set up your own packaging line to enter this field. A custom filler near you has the knowledge and equipment to help in every area, from planning through production.

If you don't know the name of a custom filler, write Du Pont. We'll send you a list and include survey data on your market for aerosol products, plus information about Freon* propellents for aerosols. "Freon" is preferred by custom fillers and is used in more of today's aerosols than any other propellent. Write E. I. du Pont de Nemours & Co. (Inc.), "Freon" Products Div. 3412, Wilmington 98, Delaware.

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*Freon and combinations of Freon- or F- with numerals are Du Pont's registered trademarks for its fluorinated hydrocarbon propellents

News in Packaging . . .

P.I. Organizes Folding Carton Committee

L. H. Zahn of Ciba Pharmaceutical Products, Inc., and director of committee activities for the Packaging Institute, Inc., has announced plans for a Folding Carton Committee in the Materials Division, which is headed by W. B. Tibbets, Union Carbide Plastics Co., and S. B. Smith, The Dow Chemical Co. Launching chairman is Marshall Baldwin, Household Products Division, Colgate-Palmolive Co.

Broad objectives of the new committee will be to develop performance (use) standards covering most of the factors involved with folding cartons, for the assistance of the user of packaging materials and machinery.

As has been done by the other 25 technical committees of the Institute, this committee is expected to provide this service by means of concentrated study in a specialized area.

Details are to be announced soon.

Vacuum-Formed Plastics

The economic advantages, usefulness, and method of vacuum forming as a technique for producing plastic products are discussed in a 20-page booklet published by the plastics division of Eastman Chemical Products, Inc., 250 Madison Ave., N. Y. C. 16. Entitled, Vacuum Forming Shapes New Markets; New Opportunities, the booklet is the third in the series of Tenite Plastics Views issued by the Eastman Kodak Company subsidiary.

Toggle-action Aerosol Valve

A. Schrader's Sons, Division of Scovill Manufacturing Co., has developed a toggle-action valve for pressure-packaged spray cans. When the button is pushed or tilted in the indicated place, the valve dispenses only straight ahead, away from the user.

Self-Dispensing Container

The Ivers-Lee Company has made available its Dispensit Package, a self-dispensing container that can handle from 10 to 1000 units, each individually packaged. Samples of tablets, capsules, powders, or liquids, in a variety of shapes and sizes, coded and printed, can be so packaged. Pressure of the thumb extends as many units as desired.

Collapsible Metal Tubes In Coming Packaging Show

The Collapsible Tube Manufacturers Council, after an absence of three years, will again have its own booth in the annual packaging show this coming April in Atlantic City.

Cooperating in the display, which will demonstrate the manufacture, wide usage, and valuable features of metal tubes, are: Art Tube Co., Atlantic Manufacturing Co., Atlas Tube Co., Michigan Collapsible Tube Co., National Collapsible Tube Company, Peerless Tube Co., Sheffield Tube Corporation, Standard Collapsible Tube Co., Turner Tube Corp., Wheeling Stamping Co., White Metal Manufacturing Co., and A. H. Wirz, Inc.

Kimble Glass Company's new square-shaped, borosilicate, volumetric flask in five sizes, to save space. The 1,000-ml size covers 38 per cent less shelf area than conventional flask. Meets Nat. Bureau of Standards specifications.

L'Oreal of Paris bleach powder in single application package of Poly-Cello by Print-A-Tube Company, which is tough, resists moisture, protects against caking and deterioration. Bleach made in U. S. A. by Cosmair, Inc., N. J.

P.I.'s Corporate Award

Ethicon, Inc., a Johnson & Johnson company, has received the Packaging Institute's 1959 Corporate Award for its surgical suture package, in which sutures are first sealed, then sterilized by electron beam.

New line of products by Podiatrex, Ltd., of Glendale, Calif. for podiatrists' and chiropodists' prescriptions, five ethical pharmaceutical specialties now being detailed to practitioners of U. S., Canada and the Philippines.

Stanback Company's cellophane bundling of its new tablet package designed by Koodin-Lapow Associates. Cellophane is Olin 450 MST-54 by Packaging Division, Olin Mathieson Chem. Corp.; printing by Charlotte Carton Co.

Ethicon's surgical suture package sterilized by electron beam, developed with Dobeckmun Co. utilizing Metalam by Dobeckmun, a combination of aluminum foil, vinyl plastic and paper for strength, imperviousness to liquids, gases.

your product belongs

in glass by Brockway

What makes a product belong? Acceptance by the consumer public . . . acceptance for the product itself . . . and acceptance for the container in which it is presented for sale. • A good product is greatly enhanced at the point of sale when presented in an attractive glass container . . . a glass container by Brockway. • Brockway provides individuality in a glass container . . . the kind of individuality that makes your product stand apart from all the rest, thereby providing a strong advantage at the point of sale. • A product that is worthy of consumer acceptance deserves a quality glass container by Brockway.

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Tygart Valley Glass Co., Washington, Pa.

NEWS and VIEWS

BY TED KLEIN PUBLIC RELATIONS DIRECTOR*

PR on the Carpet

The sound and the fury of the TV quiz scandal have not as yet died down. I think that neither the public nor the industry (advertising, TV, or sponsors) will ever be allowed to forget these incidents. I am concerned that the words "public relations," "publicity," and "press agent" have once more been used to imply categorical dishonesty. An article in one paper told, in detail, of how a "press agent" bribed TV producers to put an employee of one of his firm's clients on a quiz show. Outsiders must get the impression that this profession, of which I consider myself a member, is one step below that of the world's oldest. Naturally I can't agree. So, to set the record straight, here is a statement from this corner on the role of public relations and the present mess in TV.

Many businessmen employ the services of individuals skilled in the art of communication. Their principal job is to place in the most favorable light a client's company, its people, and its products. Success in this *never* requires that the expert in communication resort to questionable practices involving, deceit, bribery, or misstatement of fact. Those who do turn to these devices are charlatans, unskilled in their craft. The public is rightly shocked about the present standards of morality in many phases of the entertainment industry. There are far more individuals in public relations who refuse to "play the game." Those who do play it are truly despicable, but let's consider the majority who will not be corrupted, before we burn down the house to destroy the rats.

Kudos to Seagram

One of the most difficult assignments for a public relations man is that of getting publicity on an inanimate object like a new building.

A. A. Schechter Associates of New York recently faced this problem in publicizing the dedication of Seagram's new headquarters in New York City. Their big idea was to let the dedication serve as the reason for a symposium at the Waldorf-Astoria on "The Future of Man."

Panelists included Robert Frost, Pulitzer Prize-winning poet; Sir Julian Huxley, author and biologist; Lord Bertrand Russell, Nobel Prize-winning philosopher; Dr. Hermann J. Muller, Nobel Prize-winning zoologist; Devereux Josephs, chairman of the President's Committee on Education Beyond High School; and Dr. Ashley Montagu, well-known anthropologist and social scientist.

Each of the panel members spoke, Lord Russell giving his talk via video tape from London, and was then interviewed by newsmen Douglas Edwards, William L. Lawrence and Inez Robb. Dr. Milton Eisenhower, chairman of the symposium, acted as moderator for the stimulating question period which followed the presentations by each of the panel members.

Over 1200 invited guests heard the symposium at lunch, and an estimated 500,000 heard it broadcast a few days later over the CBS radio network.

It was an exciting and novel way to celebrate the dedication of a building devoted to business, and one which will long remain in my memory as a definite, sane contribution to the confusion of this age.

Every Third Person

The United States Office of Education estimates that by the end of this year 46.5 million full-time students will be enrolled in elementary, secondary, and higher education. College enrollment is now 190,000 more than last year, at a new high of 3,780,000. Adding another 8,270,000, the number of people who take part-time training at schools, gives a total enrollment of 54,750,000. This means that one out of every three people in our country is going to school.

Postgraduate Education

The Institute for Advancement of Medical Communication, in New York, is attempting to do something about the fast-growing field of medical television as it relates to postgraduate education of physicians. At a recent conference sponsored by the Institute, in Bethesda, Maryland, some 125 registrants from all phases of medical communication gathered to discuss the problems involved.

The meeting opened with a keynote address on closed-circuit TV from Arthur S. Flemming, Secretary of the Department of Health, Education and Welfare, in which he called attention to the fact that the greatest weakness in medical care and preventive medicine lies in the problem of continuing medical education for practicing physicians.

The subjects of the two-day conference were model plans using TV, including open-circuit, closed-circuit, and "private" or coded telecasts to special audiences. There was also discussion of equipment, personnel training, and problems of financial support for TV projects.

Since many medical schools are now using TV in some way to provide information to physicians, a study was made by the Institute to determine just what was being done, and how wider cooperation might further the over-all goals of medical television. As of now, some 32 of the 85 medical schools in the country have, or will shortly have, going TV operations.

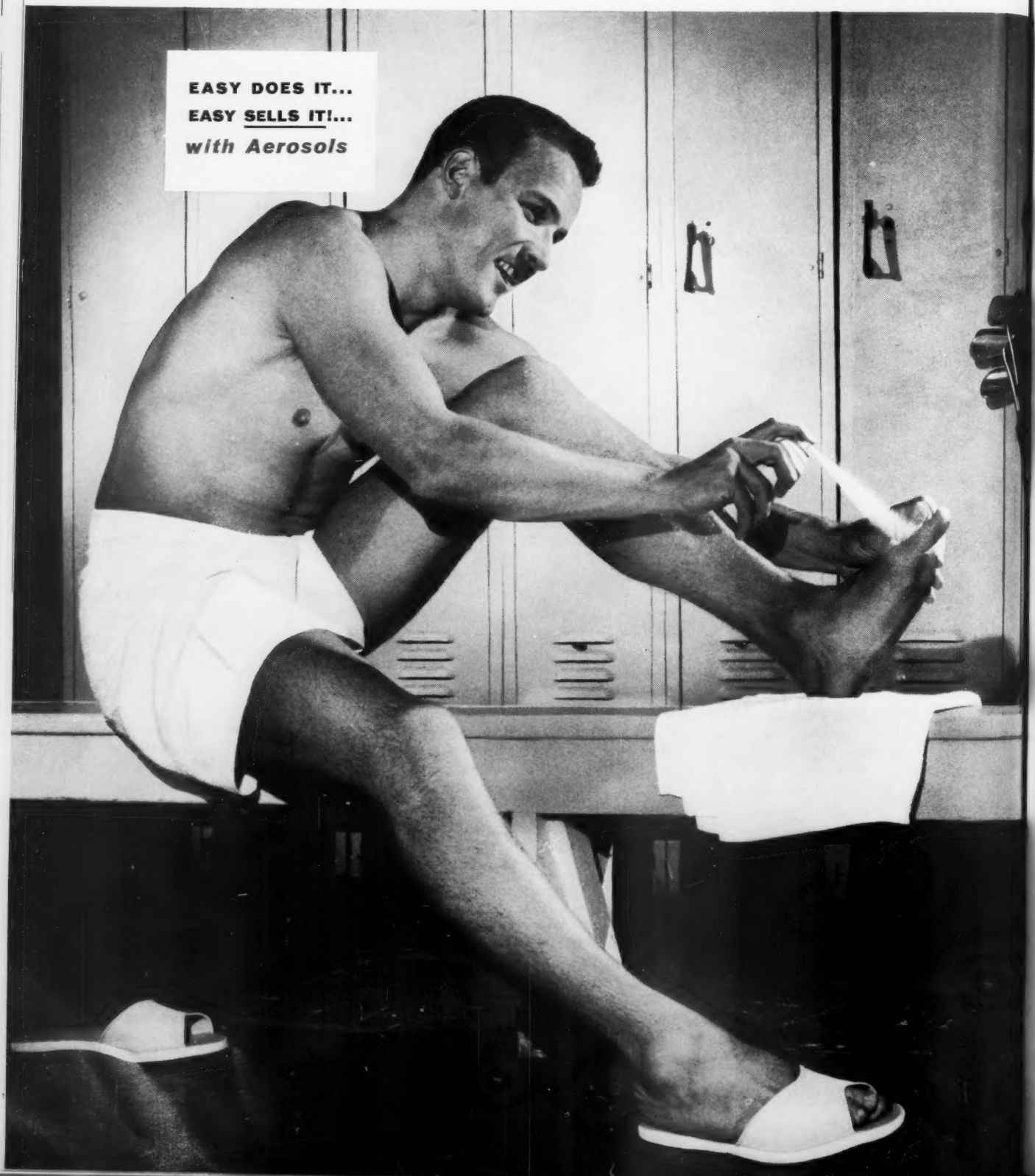
The conference adjourned with the decision to meet again in the Spring of 1960 to discuss further these same issues. For complete information on what medicine is doing in postgraduate education via TV, I suggest you write to Richard H. Orr, M.D., Executive Director, The Institute for Advancement of Medical Communication at 33 East 68th St., New York 21, N. Y.

Going Up

Bill Auchincloss, president of Schnell Publishing and a bit of a seer, told a recent Young Men's Board of Trade luncheon that 1960 will be the biggest year yet for our industry. Sales in 1959 will be about 1.8 million dollars and, according to the editor of *Oil Paint & Drug Reporter*, 1960 sales will be around 2 billion. The chemical industry has come a long way from the 1946 annual sales of 11 billion to last year's 25. Auchincloss reports that in 1960 cardiovascular drugs, vitamins, and tranquilizers will continue to lead the pharmaceuticals, with antihistamines taking 20 per cent of the total.

*Paul Klemtner & Company, Inc.

The Magic Touch of



Aerosol Packaging

could be your Rx for bigger pharmaceutical sales

Ever ask yourself these questions? *Would my pharmaceutical product be "better" as an aerosol? Would aerosol packaging make it easier to use or more acceptable? Would it generate more sales? Would it yield a better margin of profit?* Chances are, if your product can be sprayed, poured, dusted or daubed the answer to all these questions is *yes!*

Last year, pharmaceuticals were the fastest growing of all aerosol product groups—showing a sales increase of 50% in 1958 over 1957, compared to a 20% increase for all aerosols. And the market is still growing fast. It is expected that sales will reach $200 million by 1961!

Many Sales Advantages

There are many reasons for the success of aerosol-packaged pharmaceuticals. They deliver the product in a completely new form that's easier to dispense and apply, more convenient and more pleasant to use. They never are affected by evaporation of active ingredients or vehicles. They are cooling and dry rapidly on the skin. They are aseptic—untouched by the hands in applying. And they produce a minimum of irritation to the treated area. They can be inhaled easily and will penetrate nasal passages and bronchial tracts more effectively, thus speeding up the effects of medication.

Right now's the time to plan on capturing your share of the booming aerosol pharmaceutical market. And to help you get started in aerosol packaging of your medicinal product—General Chemical offers many valuable services:

Forward Research

As an extension of its own aerosol research and development program, General Chemical has initiated a grant-in-aid program at a large eastern college of pharmacy expressly for the study of pharmaceuticals in aerosols. Such research on all phases of pharmaceuticals as aerosols will help accelerate development of many new products.

New Product Ideas

Advance research in our aerosol laboratories has led to the development of typical formulations for a number of new or improved aerosol products. We are currently mailing out a New Product Bulletin each month. If you'd like to receive these bulletins, just ask us to add your name to our regular monthly mailing list.

Contract Fillers

We will also be glad to put you in touch with highly capable contract fillers, who can put up small test runs for you or handle full-scale commercial production. They will work with you from planning and testing through to volume filling. You don't have to invest a cent in equipment or production personnel when you work with these contract fillers!

For further information—or if you would like to arrange for a special presentation—write today to "Genetron" Dept., General Chemical Division, Allied Chemical Corporation.

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Patent thoughts and trends

BY THOMAS CIFELLI, JR., PATENT ATTORNEY*

New Areas of Patent Protection

The writer has often wondered about the amount of patent protection lost to workers in the drug and cosmetic fields simply because such protection has been overlooked. Reference is made to protection in fields allied with the drug and cosmetic fields. Examples of such allied fields would include those involving the use of agricultural chemicals and animal feed compositions.

One can almost hear the immediate reaction of the reader: a person should stick to his own last and, anyway, it would be impractical for workers in the drug and cosmetic fields to seek protection in other fields. The short answer to these two points is that one does not have to go outside his own field of knowledge to obtain such protection; and, secondly, it does not necessarily follow that it is impractical to obtain protection in allied fields. Brief support of these points will now be made.

Workers in the drug and cosmetic fields can obtain patent protection in related fields in a practical way. Different avenues are offered such workers. For one thing, they may collaborate with various public agencies, such as departments of the U. S. Department of Agriculture or any one of the numerous excellent agricultural experimental stations. Then too, collaboration with consulting or testing firms is available. A further practical solution of the problem is collaboration with commercial organizations in the related fields in question. Such organizations have all the know-how required in those fields. Another solution to the problem is the creation of another department in the drug and/or cosmetic workers' organization. This solution does involve going outside of the drug and cosmetic fields, but is perhaps the best solution where the amount of work is great enough to support this method. That this is true in a number of cases is shown by the fact that a number of drug and cosmetic companies do have divisions or departments concerned with agricultural and/or animal applications.

When one considers the tremendous rewards available in the agricultural and animal feed areas, it really is a wonder that these fields have been left relatively untouched by workers in the drug and cosmetic fields. The amount of materials used in agricultural areas and in animal feeds is of a much higher order than workers in the drug and cosmetic fields normally comprehend. One must think in terms of large tonnages rather than in just pounds.

That there are a number of people who are thinking, perhaps for the first time, of protection in just the two areas mentioned is believed to be self-evident from the increasing number of patents being issued in those fields. This statement is admittedly made on the basis of the impressions gained by the writer in going over patents issued by the United States Patent Office during the past 20 years. It is believed that this impression is correct, even though no effort has been made to make a statistical study of the situation.

Perhaps one word of caution should be inserted at this point. If any collaboration is entered into, and one deals with another party on matters that might give rise to patent rights, it is always best to have a clear understanding at the outset with respect to how the patent rights are to be owned. Otherwise, disagreement may result if a meritorious or commercial finding is made. Anyone who knows anything about controversies and the chances of amicable settlements will agree that the best way to have amity is to *avoid* the controversy.

Recent Patents on Growth Stimulants for Animals

Among the many patents dealing with animal feeds just three have been selected as illustrations to indicate the scope of protection available in this field.

An inventor connected with the Iowa State College Research Foundation recently obtained U. S. Patent No. 2,906,621 on his basic finding that very young baby pigs have incomplete enzyme systems, particularly being deficient in proteolytic enzymes. By compensating for this deficiency the inventor was able to effect an increase in the rate of weight gain and also in the feed efficiency.

Heretofore, according to the inventor, the practice was to allow baby pigs to nurse the sow until they reached eight or ten weeks of age. This resulted in a relatively inefficient feed utilization, since the feed had to be first fed to the mother hog to produce milk for the baby pigs. The method of raising pigs on sows also produced a heavy loss of baby pigs. In the past, about one-third of all live pigs farrowed died from some cause or other before they were weaned at eight to ten weeks of age. Current estimates still place this figure as high as 25 per cent, on the average. Moreover, the baby pigs that survive usually weigh only from 28 to 30 pounds at weaning age (eight weeks). The development of synthetic liquid milk for baby pigs was one approach to this problem, but the high costs of synthetic milks and the difficulty involved in their feeding and management made them impractical. In 1953, the Iowa Agricultural Experiment Station found it possible to wean pigs as early as one week of age and to feed them a dry nutritionally-balanced ration called a pig pre-starter. Also, the practice is followed of letting the pigs nurse sows while supplementing the sow's milk with a so-called "pig-starter" in a creep from one to eight weeks of age.

J. C. Lewis won a patent for the Secretary of Agriculture on his finding that certain strains of the species *Bacillus subtilis* have the ability to biosynthesize nutritional factors useful for stimulating the growth of chicks and other animals.

*Richards and Cifelli, Newark 2, New Jersey.

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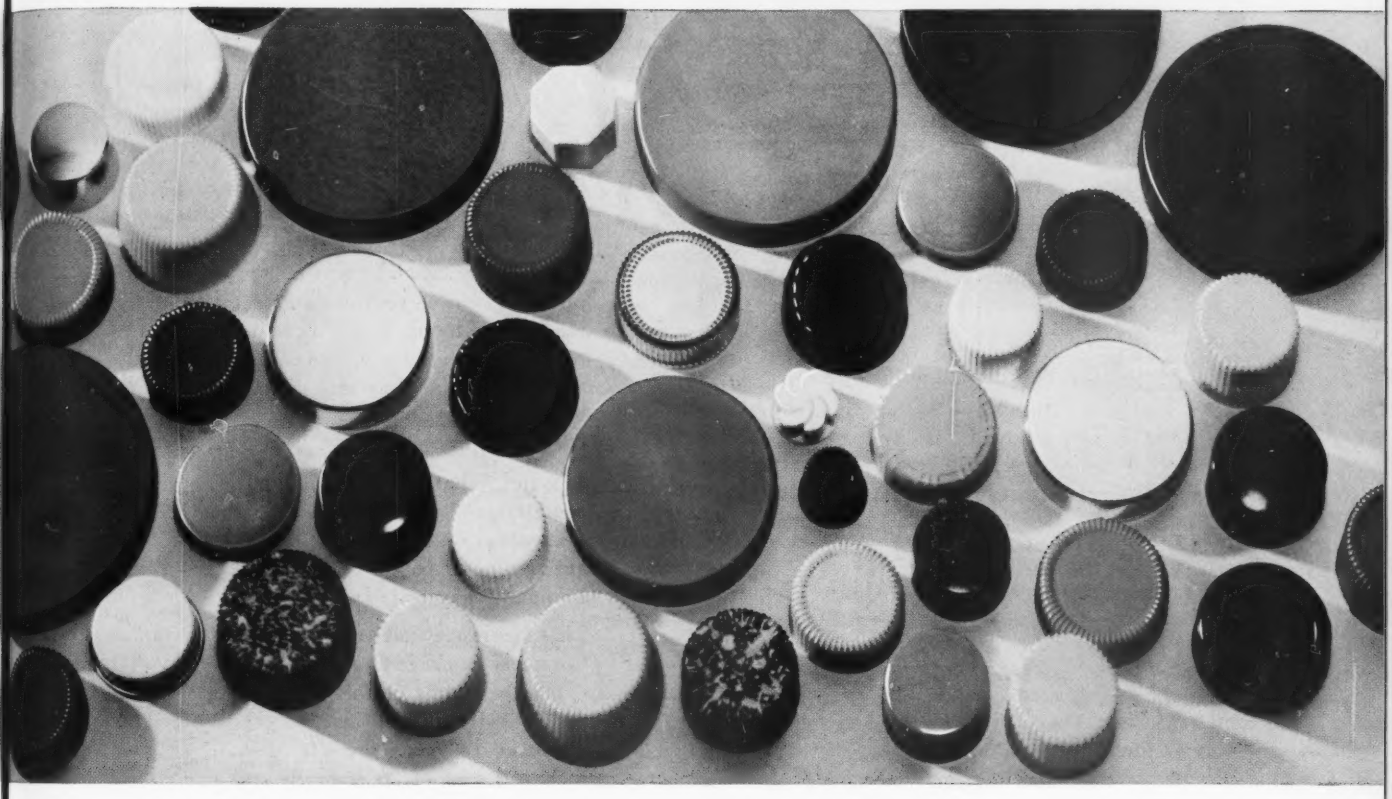

Owens-Illinois Closures add to the sales appeal of your package

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Owens-Illinois closures add beauty, but of equal importance is their durability and resistance to most chemicals . . . providing the ideal closure for almost any product.

Plastic and metal closures are but one part of the Owens-Illinois Complete Packaging Approach . . . the right container, attractive label design, special fitments, and merchandising carton.

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Here, at the crucial point of purchase—when your aerosol product reaches the hands of the ultimate consumer—the importance of having your private label aerosol made by G. Barr & Company becomes apparent.

It is here that the more than 60 production line inspections and the meticulous quality controls that are routine at G. Barr & Company, pay off!

This assurance that your G. Barr & Company packaged product will reach the hands of the consumer perfectly formulated and packaged is backed by our technical staff of 20 research and product development chemists, by our two plant production efficiencies and by the fact that we maintain the strictest standards of quality in the industry.

If you believe your product deserves the utmost in packaging proficiency—yet at no increase in cost—ask us to outline the many advantages of our service for you.

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According to the patentee, the exact method by which the cultures work is not known. In the words of the patentee:

"Thus cultures of these microorganisms, or concentrated preparations thereof, when fed to animals give growth responses which cannot be attributed to any of the known growth factors or to antibiotics which have been described previously and which have been described previously and which have been recognized to be nutritionally active. It is not yet known whether the individual strains elaborate similar or different nutritive factors. Also it is not known as yet whether the growth stimulating properties of these strains are due to their antibiotic constituents or constituents of a vitamin character such as the unknown nutritive factors in fish solubles, whey, grass juice, etc. Regardless of the nature of the growth-promoting substances, whether they ultimately prove to be of an antibiotic nature or of a vitamin nature, or unlike either of these types, the fact of the matter is that cultures or concentrates of these strains give growth responses that have practical significance as shown in the examples hereinafter.

"The organisms used in applying this invention are two strains of *Bacillus subtilis* which are described as follows: One of the strains is that described as No. 231 by Smith, Gordon, and Clark (Aerobic Spore-forming Bacteria, Dept. of Agriculture Monograph #16, November 1952, page 74). This strain is also on deposit in the culture collection of the Northern Regional Research Laboratory, Peoria, Ill., as NRRL B-543, and in the American Type Culture Collection, Washington, D.C., as ATCC 6633. This strain will be referred to herein by the latter designation. The other strain of *B. subtilis* is on deposit at the Northern Regional Research Laboratory as NRRL B-1467. Both the ATCC 6633 strain and the NRRL B-1467 strain produce subtilin and exhibit the same antibiotic patterns. On the basis of these and other observations it is believed that the two strains are very closely related and may even be identical."

The Lewis patent is U. S. 2,906,-622.

A third patent showing a more direct chemical approach to animal feeds is No. 2,907,658, assigned to Chas. Pfizer and Co. This patent covers the use of ascorbyl benzoate in animal feeds. The inventor, H. G. Luther, points out that the nutritional value of ascorbic acid, that is, vitamin C, is well known for man and certain animals, for example monkeys and guinea pigs. Rhesus monkeys are singled out as extremely important, since they are used in the production of the Salk polio vaccine. The problem with vitamin C has been its lack of stability on account of its ready oxidation, the resulting products suffering a loss of vitamin C activity. According to Luther, not only is ascorbyl benzoate a suitable source of vitamin C activity, but he has also found it to be an anti-oxidant which meets the rigid requirement of non-toxicity in food and feeds. This rigid requirement has eliminated many of the more common effective anti-oxidants in use in products consumed by man and animals. Another property of ascorbyl benzoate is that it possesses inhibitory activity against microorganisms which are presumed to be involved in rancidity development in food and feeds containing fats. An example showing the use and superiority of ascorbyl benzoate over ascorbic acid is given below, as taken from the patent:

"To one pound samples of a typical feed mixture containing the following ingredients:

White corn meal	lbs.	82.5
Soybean oil meal (44% solvent extracted)	lbs.	37.5
Wheat middlings	lbs.	15.0
Whey	lbs.	4.5
Meat scraps (50%)	lbs.	4.5
Ground limestone	lbs.	2.5
Dicalcium phosphate	lbs.	2.4
Salt, iodized	lbs.	0.75
B_{12} (10 mg./lb. supplement)	gms.	20.44
Manganese sulfate	gms.	18.0
D_3(Delsterol 1500 u./gm.)	gms.	34.0
Choline chloride (25%)	gms.	187.5
Vitamin E (Myvamix, '0,000 u/lb.)	gms.	15.3
Niacin, U.S.P.	gms.	1.2
Thiamine hydrochloride U.S.P.	mgs.	135.0
Riboflavin U.S.P.	mgs.	240.0
Calcium pantothenate	mgs.	217.6
Pyridoxine hydrochloride, USP.	mgs.	250.0

was added 1.65 grams of ascorbyl benzoate, 1 gram ascorbic acid U.S.P. by premixing these amounts in 20 grams of the feed and adding to the remainder. The mixtures were then blended for 20 minutes. Ten gram samples were used for the initial assays for ascorbic acid acivity by titration with 2,6-dichlorophenol indophenol dye solution. Bulk samples of this mixture in cloth bags were held in an oven at 30° C. and 70 per cent relative humidity. Assays for ascorbic acid activity were made at weekly intervals. The assay of feeds for ascorbic acid were performed by adding 100 ml. of 3 per cent metaphosphoric acid solution to 10 grams of feed in a 250 ml. flask, shaking for one minute to dissolve the ascorbic acid and filtering to obtain a clear filtrate. Five milliliters of the clear filtrate was then titrated to a permanent pink color. A titration blank containing ascorbic acid free feed was then substracted.

"The assay of feeds for ascorbyl benzoate was performed in the same way employing a 3 per cent metaphosphoric acid solution containing 2 volumes of water and 1 volume of acetone. The results based on the retention of the ascorbic acid activity as given in Table I.

Time, Weeks	Ascorbyl Benzoate, percent retained	Ascorbic Acid U.S.P., percent retained
1	96	92
2	94	80
3	90	80
4	84	60
5	81	40.5
6	79	32
7	77.5	24
8	82	.....

From these results, the stability of ascorbyl benzoate over ascorbic acid is obvious."

An interesting feature of protection in the field of animal feeds is that, even though the compound used as the additive may be old, it is not a difficult matter to obtain adequate, that is, broad, protection. This is unlike the situation with respect to drugs and cosmetics in general. The Patent Office in the latter two cases almost always requires the inventor to claim his invention in a rather specific manner, although a certain amount of latitude is given in some cases. However, claims covering the additives very broadly in conjunction with animal feeds are commonly granted by the Patent Office. As an example, consider claim 1 of U. S. Patent No. 2,904,658—"An animal feed composition which comprises a nutritionally balanced feed together

(*Continued on page 842*)

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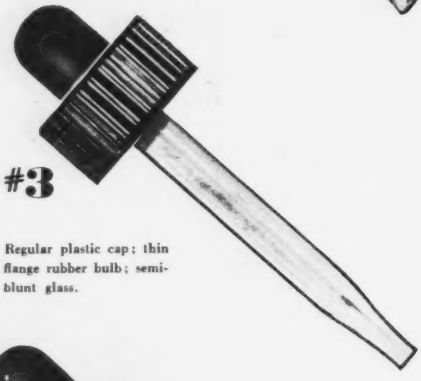
#1

Non-rolling, extra-depth, Bakelite cap; thick-flange rubber bulb; Saftee-ball glass.



#3

Regular plastic cap; thin flange rubber bulb; semi-blunt glass.

#4

Metal cap; AMEKINE oil-resisting synthetic rubber bulb; blunt glass.

They're A-1 with your customers, too . . . assuring you repeat sales!

When you sell a product that pleases and satisfies your customers, you're assuring yourself of their goodwill and continued patronage. New Perfection Dropping Parts help to give you that kind of a product. They are convenient, attractive, dependable—manufactured and assembled under careful and constant inspection to assure the highest possible quality.

RUBBER BULBS are supplied in many styles and colors. Oil-resisting AMEKINE synthetic rubber is used for oil preparations; natural rubber is supplied for other products.

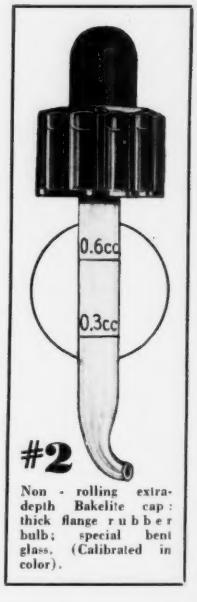
CAPS of plastic or metal can be furnished in a complete range of sizes and colors.

DROPPER GLASSES are available in a wide variety of styles and sizes; plain or CALIBRATED in any color to mark specific dosages.

• • • • •

We can make up dropping parts to fit your own bottles or we can supply bottles in an attractive modernistic style in Amber, Blue, Green, or Clear glass, complete with dropping parts, in the following sizes: 1/8, 1/4, 1/2, 1 and 2 oz.

• • • • •



#2

Non-rolling extra-depth Bakelite cap; thick flange rubber bulb; special bent glass. (Calibrated in color).

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PENNSYLVANIA
GLASS PRODUCTS CO. INC.

"Glass Goods of the Better Kind"

430 N. CRAIG ST. • PITTSBURGH (13), PA., U.S.A.

Reap Sales Gold with the New Richford Metallic Finishes!

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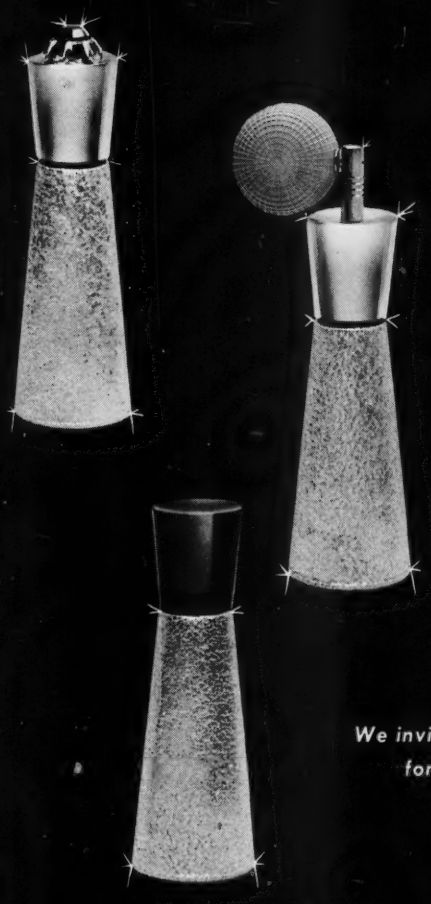
. . . the new precious finish
applied to our plastic closures to give your product
that air of priceless beauty!

Available "at once" in all sizes from Richford's unique stock selection of caps and closures in the popular Flare, Futura, Square shapes and Ambassador style . . . in both standard and spillproof styles. Can also be applied to your own closures . . . any size . . . any shape.



"Gold Mist"

. . . the companion precious finish applied to our glass containers for outstanding beauty, durability and elegance. Available in our "Exquisite Flacons" in both standard and spillproof styles.

We invite your inquiries for samples and prices.

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...because Givaudan is a wholly integrated international organization with manufacturing, creative and compounding facilities in full operation in several of the world's major perfume and cosmetic marketing areas.

No matter where your foreign plants are located, you are always assured of the same high standards of Givaudan quality and service, backed by careful coordination at every technical level... production, quality control, technical service and new product development.

GIVAUDAN-DELAWANNA, INC.
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From left to right: E. Lynch Smith, who has been elected secretary of the National Can Corporation; Dr. Thomas C. Fleming, medical director of the Warner-Chilcott Laboratories Division of Warner-Lambert Pharmaceutical Company; John Garizio, now vice-president as well as assistant to the president, at the Reheis Company, Inc.; and George L. Wolcott, M.D., who has joined Wallace Laboratories as scientific director.

NEWS . . .

Appointments and Promotions

E. Lynch Smith, who recently left the law firm of Frost & Jacobs to join **National Can Corporation,** has been elected secretary of that firm.

Dr. Thomas C. Fleming has been appointed medical director of the **Warner-Chilcott Laboratories Division of Warner-Lambert Pharmaceutical Company.** Dr. Fleming was formerly director of product development at Mead Johnson & Company.

Reheis Company, Inc., has appointed John Garizio vice-president, in addition to his position as assistant to the president. He has been with the firm for 11 years.

George L. Wolcott, M.D., has joined **Wallace Laboratories** as scientific director. He was previously medical director and assistant vice-president of Bristol-Myers Products Division and director of industrial health for Bristol-Myers Company.

Roche Laboratories, Division of Hoffmann-La Roche Inc., has promoted three marketing analysts to the following positions: Robert P. McGrath to product manager, Robert C. Bennett to assistant director of the marketing research department, and Joseph E. Debiak to product manager.

Miles Laboratories, Inc., has reorganized its legal operations into two departments, the legal department, headed by Edward D. Downing as legal counsel, and the patent department, headed by K. M. LeFever as patent counsel. Mr. Downing joined Miles in 1955, Mr. LeFever in 1956.

Edward A. Coleman, plastics sales representative in the New York office of the **Closure and Plastics Division of Owens-Illinois Glass Company,** has been appointed Eastern manager-closure sales. Frank M. Harris has been assigned to the New York office as plastics sales representative. He had been in Toledo as merchandising coordinator.

The new **Flexible Packaging Division of Chippewa Plastics Company, Division of The Rexall Drug and Chemical Company,** has Paul L. Florence as plant manager and John F. Pandolfo as division sales manager. Mr. Florence was plant superintendent of the Salinas operation and Mr. Pandolfo joined the new division two years ago when it was known as Package Containers, Inc.

S. Lee Horning has been appointed department head of the control laboratory of the **S. E. Massengill Company.** Mr. Horning joined Massengill in 1948, and has served as assistant to the department head since 1956. Lloyd L. Pair, with the firm since 1945 and assistant production manager since 1956, has become production control manager, and Francis S. Taft is now plant superintendent. He joined the firm in 1938, and since 1948 has been chief chemist, control laboratory.

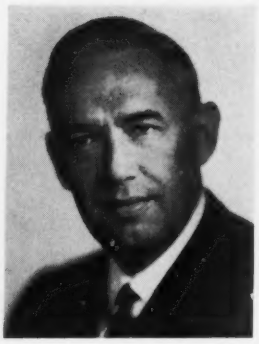
The **Allen B. Wrisley Company** has announced the following appointments to its executive staff: Marvin B. Buehlmann, secretary-treasurer; John M. Bratton, assistant to the president; George M. Klaus, plant manager; Walter M. Guzy, purchasing agent; Leonard G. Wargo, production planning manager; and Marvin Strauch, manager of traffic, receiving, shipping, and warehousing. All are promotions.

Raymond F. Fagan has been appointed director of public relations for the **Schering Corporation.** He had been a member of the public relations department since its organization in 1955, having joined Schering management research department in 1954.

The **Toilet Articles Division, Colgate-Palmolive Company,** has appointed Marshall Ward, formerly manager of market research, to product manager, succeeding Paul Byrne, who is now new products manager. C. Guy Grace, vice-president and general manager of the division has been elected to the board of directors of the Colgate-Palmolive Company. Mr. Grace has served the firm since 1929 in various executive positions.

Donald R. Thorp, who joined **Maltbie Laboratories Division, Wallace & Tiernan Inc.,** in 1947 as a sales representative, has been promoted from his position as manager of district 15 to assistant sales manager.

The **Harchem Division, Wallace & Tiernan,** has added five to its staff: William C. Wiley, who has served with Borden and Reichhold and Nopco, is product development manager; William G. Paul, formerly with Victor Chemical Works and Van Ameringen-Haebler, is representative for fatty acids in Illinois, Missouri, and Wisconsin; C. John Ebbrecht is representative for fatty acids in New England and New York State; Wallace E. Riffelmacher, formerly with Du Pont, is sales representative for chemicals and plasticizers in New England and New York; and Raymond C. Wolfert, previously with McKesson & Robbins, Inc., is sales representative for plasticizers in the mid-West.



Left to right: New appointments at International Flavors & Fragrances Inc.: George H. Cadgene, director of purchases, domestic operations; Henri van Mameren, general manager, and Dr. James H. McGlumphy, technical director in charge of research, manufacturing, and product control, both of the Flavor Division; Dr. Joseph V. Swintosky, newly appointed principal research pharmacist, Smith Kline & French Labs.

International Flavors & Fragrances Inc. has announced four new appointments. George H. Cadgene, formerly with Trubek Laboratories, is director of purchases for domestic operations, supplanting Robert L. Stickney, who has been named assistant to the president in a staff capacity. In the **Flavors Division,** Henri van Mameren, formerly managing director of the firm's Paris subsidiary, has become general manager, and Dr. James H. McGlumpy has been named technical director in charge of research, manufacturing, and product control. Dr. McGlumphy has been with the company for more than 25 years.

Dr. Joseph V. Swintosky, Ph.D., has been appointed principal research pharmacist at **Smith Kline & French Laboratories.** He had been a group leader in the pharmaceutical research section. Dr. Swintosky served as assistant professor of pharmacy at the University of Wisconsin after taking his Ph.D. degree there, until he joined SK&F in 1953. He now also serves as a visiting professor at Temple University's School of Pharmacy in Philadelphia.

Lloyd C. Bender, for the past two years field sales manager for Sherman Laboratories, has been appointed sales manager of the **Pharmaceutical Laboratories Division, Schieffelin & Company.**

U. S. Industrial Chemical Company, Division of National Distillers and Chemical Corporation, has named Joseph G. Longstreth manager of the St. Louis sales office. Mr. Longstreth has been a sales representative in that area since joining U.S.I. in 1955. Roy A. Parker, with the firm for 33 years, most recently as manager of the company's Kansas City sales office, is now Kansas City sales division manager, and John A. Putnam, a U.S.I. salesman in Atlanta for the past two years, is now manager of the Atlanta office.

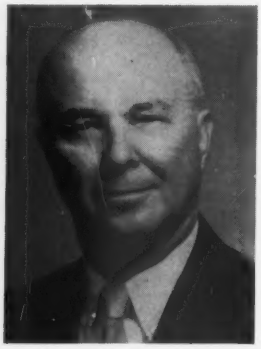
Sidney J. Natkin has joined **Helene Curtis Industries, Inc.,** as a marketing executive. He was formerly a vice-president and account supervisor with Gordon Best Company, Inc.

Girard R. Adams has been appointed as a sales and technical representative by the **Continental Chemical Company.** Mr. Adams was previously a sales representative for the Antara Chemical Division, General Aniline & Film Corporation. In his new position, Mr. Adams will cover metropolitan New York, New Jersey, and eastern Pennsylvania.

Edmund C. Gaulden, M.D., an instructor of clinical medicine at Yale University School of Medicine and a former practitioner in Branford, Conn., has been appointed associate medical director of **J. B. Roerig and Company, Division of Chas. Pfizer & Company, Inc.** Dr. Gaulden will continue his affiliation with the Yale Medical School.

The **Wm. T. Thompson Company** has appointed Douglass Henderson vice-president, operations and systems. Mr. Henderson has been for ten years with the Univac division of Remington-Rand, most recently serving as a management consultant for systems and automation in office operation and procedures.

Left to right: Lloyd C. Bender, sales manager of the Pharmaceutical Laboratories Division, Schieffelin & Company; three new appointments at U. S. Industrial Chemicals Company, Division of National Distillers and Chemical Corporation: Joseph G. Longstreth, the manager of the St. Louis sales office, Roy A. Parker, the Kansas City sales division manager, and John A. Putnam, who is now manager of the Atlanta office.



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Left to right: Paul V. Newland, M.D., director of the medical research and professional services section of Eaton Laboratories; Robert J. Elkin, marketing research director, a newly created position at A. H. Robins Company Inc.; Joseph T. Hanlon, manager of advertising and sales promotion, Crown Cork & Seal Company, Inc.; and Paul W. Roder, who is vice-president of marketing at Ciba Pharmaceutical Products Inc.

Paul V. Newland, M.D., has been named director of the medical research and professional services section of the **Eaton Laboratories Division, Norwich Pharmacal Company.** Dr. Newland has been an instructor at the University of Rochester Medical School and a member of the staff of the Strong Memorial Hospital and Rochester Municipal Hospital.

Robert J. Elkin has been appointed to the newly created position of marketing research director at **A. H. Robins Company, Inc.** Before joining Robins, Mr. Elkin worked in the marketing research department of another pharmaceutical company.

The new manager of advertising and sales promotion at **Crown Cork & Seal Company, Inc.,** is Joseph T. Hanlon, who has been with the firm's advertising and sales promotion for 20 years, most recently as sales promotion manager of the entire company.

Paul W. Roder has been appointed vice-president in charge of marketing for **Ciba Pharmaceutical Products Inc.** He joined Ciba in 1942, and has served most recently as vice-president in charge of advertising. The company has also appointed Dr. Sam Barkulis director of microbiological research, to succeed Dr. Rudolf L. Mayer, who retired last July. Dr. Barkulis had been on the faculty of the College of Medicine at the University of Illinois, first in the department of biological chemistry, and more recently in the department of psychiatry.

Mead Johnson & Company Research Laboratories has appointed Dr. Richard T. Arnold to the newly created position of director of research, to create and execute the chemical, biochemical, and biological research programs. Since 1955 Dr. Arnold has been administrator of the basic science program for the Alfred P. Sloan Foundation in New York City. He. will assume his new position in 1960, as soon as his replacement at the Sloan Foundation can be trained. During this interval Dr. Arnold is serving as a consultant to the company. The **International Division** has appointed Dr. Ludwig K. Backman associate medical director. He had been medical director of Knoll Pharmaceutical Company for four years. Dr. Bachman, born in Germany, served in residence at University Hospital, Wuertzburg, and at the Physiological Institute, Heidelberg, and, before coming to the U. S. A. in 1952, he was employed as a civilian physician with the U. S. Naval Forces in Heidelberg, Germany.

Catherine R. Ready, assistant director of Bristol-Myer's educational department, has been appointed to the newly created post of director of health and beauty services for the **Bristol-Myers Products Division.**

Wallace T. Drew, vice-president in charge of marketing, **Coty, Inc.,** has been elected to the company's board of directors. Seymour S. Sitzman has joined Coty as north eastern regional manager. He had been field manager for Johnson & Johnson.

Carl J. Siefering, formerly plant superintendent at Lanpar Company, has been appointed tablet production manager, **Marion Laboratories.**

Left to right: Dr. Richard T. Arnold, director of research, Mead Johnson & Company Research Laboratories; Catherine R. Ready, director of health and beauty services, Bristol-Myers Products Division; Wallace T. Drew, newly elected to the board of directors, Coty, Inc.; and Carl J. Siefering, who has been named tablet production manager of Marion Laboratories' newly expanded pharmaceutical manufacturing facilities.

Union Carbide Chemicals Company, Division of Union Carbide Corporation has announced five appointments in the technical service laboratory: Howard D. Cogan, Charles E. Colwell, research supervisors; John H. Fager, head, department of analytical chemistry; Charles W. West, head, department of physical chemistry; and Buelah Wood, librarian. Four men have joined the chemical research department, namely, William H. Cook, Joseph V. Petrone, Edward A. Rick, and John C. Spicer. Thomas M. Tyrell and Donald W. Urban have been promoted to technical service representatives.

Rowell Laboratories, Inc., has appointed Dr. Ben E. Greenwell, formerly with Abbott Laboratories' Research Division, as research director.

Emery Industries Inc. has announced reorganization of the development and service department, with Walter T. Meinert as director. John D. Farr is manager, product development section; Robert D. Aylesworth remains manager, applications research section; and Robert H. Dhonau is coordinator of technical service activities for fatty acids.

Wyeth Laboratories has appointed Dr. Patrick T. McLoughlin to its medical division.

Samuel F. Melcher, Jr., has become group brand manager in the **Lehn & Fink Division, Lehn & Fink Products Corporation.**

Miles Reorganizes Legal Operations

The legal operations of Miles Laboratories, Inc., have been reorganized into two distinct departments, the Legal Department, headed by Edward D. Downing, legal counsel, and the Patent Department, headed by K. M. LeFever as patent counsel, with Vincent J. Romeo, vice-president and general counsel for Miles, as head of legal operations.

Chippewa Plastics Acquires California Containers Plant

Chippewa Plastics Company, a division of the Rexall Drug and Chemical Company, has acquired the Salinas, California, facilities of Package Containers, Inc. The plant will become Chippewa's Flexible Packaging Division, and will cover the range of flexible packaging.

Dow to Build Plastics Plant in Greece

The Dow Chemical Company will form a wholly owned subsidiary to manufacture polystyrene plastic in Greece. The Greek Government has approved Dow's investment in a plant to cost more than a million dollars, to be constructed when a site has been selected. Operation is expected to begin early in 1961.

The facility, utilizing imported raw materials, will be the first to produce polystyrene in Greece. Output is scheduled for the Greek market and for export. The company will be held financially by Dow Chemie A.G., of Basel, Switzerland, a wholly owned subsidiary which manages Dow investments abroad.

Chiris Executive in U. S. A.

Traveling with F. E. Shoninger, managing director of Antoine Chiris Ltd., and president of Antoine Chiris Corporation in New York, on his return from his regular quarterly visit to the British Company, was John G. Meredith, director of sales of the British Chiris company, who is visiting the U. S. for the first time.

Mr. Meredith is here principally to develop closer coordination between the two companies in servicing American companies that are expanding their operations in the United Kingdom.

Two Join Fritzsche Quarter-Century Club

George R. Fellows, in charge of Fritzsche Brothers' Atlanta branch office, and James F. Shumaker, manager of the Philadelphia branch, observed their 25th anniversaries with the firm in November, with company-sponsored champagne dinners in their respective cities, attended by members of their immediate families and their staffs. Government bonds and embossed scrolls were presented in recognition of their services.

Florasynth Vice-President Becomes Grandfather

David E. Lakritz, vice-president of Florasynth Laboratories, Inc., became a grandfather in October, when his daughter Mrs. Richard Winston and her husband announced the birth of a daughter, Lisa Faye.

Strong Cobb Arner Acquires Panpak

Strong Cobb Arner Inc., has entered the aerosol packaging field through acquiring the assets and business of Panpak, Inc. Panpak will continue operations in its Attica, New York, plant, as a wholly owned subsidiary of Strong Cobb Arner.

Dr. Joseph M. Rait, founder of Panpak in 1954, is president, Dr. Niels C. Klendshoj, chairman of the board of SCA is board chairman, and Gustav Lucie is secretary-treasurer.

M. Lemmermyer Exhibits his Paintings

The Lynn Kottler Galleries in New York City recently held an exhibit of works by Michael Lemmermeyer, president of Aromatic Products, Inc., New York, N. Y. The show included both oil paintings and water colors by Mr. Lemmermyer.

Colgate Expands Indiana Plant

The Colgate-Palmolive Company has begun a major construction program for the Toilet Articles Division at its Jeffersonville, Indiana, plant. The project, to cost more than a million dollars, includes a four-story addition to the present manufacturing building, a two-story addition to the packaging and shipping center, and a new two-story warehouse for supplies and finished products. A single-story office building will also be erected in the area.

Anca Pharmaceuticals

The Anglo-Canadian Drug Company Limited, of Oshawa, Ontario, has changed its name to Anca Pharmaceuticals, a Division of The Wander Company of Canada Limited.

Anca will manufacture and distribute the Triaminic family of products formerly sold by Smith-Dorsey Company, as well as its former products, which are to be marketed under the new company name.

Reynaud Expands

Reynaud, Ltd., has moved office, laboratory, and manufacturing facilities from New York City to new and considerably larger quarters at 900-910 21st St., Union City, N. J.

From Heyden Newport

N.F. (F.F.C.)
As an odorant in soaps, hand lotions and other cosmetics and as an additive in flavoring compounds.
TECHNICAL
Useful for the synthesis of pharmaceuticals and organic chemicals.

PREFERRED SOURCE FOR HIGHEST PURITY AND UNIFORMITY

BENZALDEHYDE

When you process with Heyden Newport Benzaldehyde, you are assured of unsurpassed purity and uniformity in the characteristics you seek—chemical reactivity, volatility, odor and taste.

That's why leading cosmetic, aromatic and pharmaceutical producers rely on Heyden Newport as their basic source for this valuable intermediate.

For new product development, as well as for those now in commercial use, it will pay you to investigate the processing benefits of Benzaldehyde and its chlorinated derivatives, such as o-Chlorobenzaldehyde and p-Chlorobenzaldehyde.

Heyden Newport Benzaldehyde N.F. (F.F.C.) or Technical is shipped in 450 lb. stainless steel drums, 100 lb. glass carboys, and 40 lb. lined drums. Samples and technical data are available upon request.

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Where tradition meets tomorrow in chemical progress

Patterson Retiring from Upjohn in January

Retirement of C. V. Patterson, executive vice-president of The Upjohn Company, from active management was recently announced, to be

C. V. PATTERSON

effective January 4, 1960. Mr. Patterson will remain a member of the board of directors and will continue to serve in an advisory capacity.

Mr. Patterson, who has been with Upjohn since 1925, is retiring at this time because of his health.

Herbert Hamilton to Receive 1959 CSMA Achievement Award

Herbert W. Hamilton, for many years secretary of the Chemical Specialties Manufacturers Association, has been selected to receive the 1959 Achievement Award of the Association, for "outstanding contributions in the field of chemical specialties."

Secretary of the CSMA for nearly 20 years, Mr. Hamilton has been, since 1950, general manager and secretary of the Association. He was president in 1928 and 1929 when the organization was known as the National Association of Insecticide & Disinfectant Manufacturers, and has served for several years on the board of governors, and as chairman of an Executive Office Committee.

U. S. Navy Cites Norwich Physician

Julius M. Amberson, Captain, M.C., the United States Navy (Ret.) was cited recently by the Bureau of Medicine and Surgery of the U. S. Navy for "exceptional service" during the past 30 years. Dr. Anderson, who is now director of medical research for the International Division of the Norwich Pharmacal Company, received the certificate at a special ceremony from Vice Admiral Thomas Coombs.

V. Burgher Retires from Ciba

Vincent A. Burgher, vice-president in charge of sales at Ciba Pharmaceutical Products Inc., has retired after 32 years with the company.

VINCENT A. BURGHER

Mr. Burgher joined the firm in 1928 as a professional service representative. In 1937 he became sales manager, and in 1942 was appointed a vice-president.

He has been active in many pharmaceutical and pharmacy associations, and is a former director of the recently merged American Pharmaceutical Manufacturers Assn.

Hurewitz Wins Wellcome Prize

Lieutenant Colonel Hurewitz, M.C., U. S. A., received the Wellcome Prize at the 66th annual convention of the Association of Military Surgeons of the United States. The prize—a silver medal, a scroll, and an honorarium of five hundred dollars—is awarded annually at the discretion of the Association of Military Surgeons, for the best essay on medico-military affairs prepared by one of its members.

The essay by Colonel Hurewitz, Commanding Officer of the Seventh Evacuation Hospital in Germany, is entitled "Military Medical Problems of the Lebanon Crisis."

The presentation, was made by Brigadier General John R. Wood, Medical Corps, U. S. Army (Ret.), who is vice-president and director of research of Burroughs Wellcome & Co. (U.S.A.) Inc.

Foragers to Celebrate in January

The Foragers of America will hold their 61st annual banquet at the Stork Club in New York City on Thursday evening, January 7th, 1960. Bill Hendry is chairman of the entertainment committee.

Seaway Chemical Corp. Formed by Kritchevsky

Jerome Kritchevsky, until recently vice-president and export manager of Stepan Chemical Company, has announced the formation of the

JEROME KRITCHEVSKY

Seaway Chemical Corporation, an export-import agency specializing in chemicals, which will also represent Stepan products in foreign markets. The new company will be at the Stepan address, 427 W. Randolph Street, Chicago, until next Spring, when Stepan moves to its new building in Northfield, Ill., at which time Seaway will relocate at 111 W. Monroe Street, Chicago.

Prior to his association with Stepan, Mr. Kritchevsky was president of Ninol Laboratories, Inc., which was purchased by Stepan in 1957.

Two Abbott Writers Receive Copywriters' Awards

Dean Carson and John Jakes, both product promotion managers in the advertising department of Abbott Laboratories, recently received "30" emblems for exceptionally high scores in the competition for the best advertising copywriting of the year from the Chicago Copywriters Club.

In addition, Mr. Carson received the first prize for the best piece of printed copy, a direct mail piece for Dayalets, one of Abbott's nutritional products.

Lilly Purchasing Virginia Plastic Container Firm

Eli Lilly and Company is purchasing the Hake Manufacturing Company, Roanoke, Virginia, makers of plastic containers, as of January 2. Plastic containers will continue to be manufactured at the Roanoke plant.

Resistant "STAPH"?
Use **G-11®** *(Hexachlorophene U.S.P.)*

Today, in hospitals throughout the country, increasing emphasis is being placed on programs for the control of staphylococcic infections. In some hospitals and communities these infections have at times approached epidemic proportions.

One important cause of this health hazard is the ease with which the staphylococci develop resistance to antibiotics.

Fortunately, these staphylococci show no resistance to G-11 (Hexachlorophene). It is one of the most, if not *the* most effective, of all commonly available antiseptics for the treatment of local infections and reducing the spread of staphylococci by preventing colonization on the skin and transmission via hands and the air.

Ask for complete technical report, "G-11 for Control of Staphylococcic Infections."

Sindar is the discoverer of hexachlorophene and its trade name "G-11" stands for the experience and knowledge gained through the years of widespread use. Our laboratories are staffed and organized to give you the benefits of this pioneer experience. Your inquiries will receive our prompt attention.

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Penick Organizes Mexican Subsidiary

S. B. Penick & Company has organized its third foreign subsidiary, S. B. Penick & Cia. de Mexico, S.A., in Mexico City. The others are in England and France.

Operations of the Mexican branch are under the supervision of A. J. Dotres, director of foreign operations, who also directs the English and French branches, from Penick's New York headquarters.

Dow Forms Saginaw Bay Division

Formation of the Saginaw Bay Division of The Dow Chemical Company has been announced by W. H. Schuette, Dow vice-president and general manager of its Midland Division. The new division groups three separate Dow operations in Bay City on a 1400-acre tract on the Saginaw River near the Bay, the petrochemicals plant, the polychemicals area, and the Bay Refining Company, two of which are now going into production.

Luis de Hoyos Presents Figurine to N. Y. Museum

Governor Nelson Rockefeller of New York State recently accepted a 2000-year-old pre-Columbian stone figurine of the Mezcala culture from Mayor Luis de Hoyos of Monticello, New York, in behalf of the New York Museum of Primitive Art, of which Mr. Rockefeller is the president and founder.

Mayor de Hoyos is also general manager of Synfleur Scientific Laboratories. He holds America's widest private collection of Mezcala stone sculpture.

Photographed at the Annual Symposium on Antibiotics, Washington, D. C., left to right: Dr. Rene J. Dubos, discoverer of Tyrothricin and Gramicidin; Mrs. Dubos; Dr. Charles E. Dutchess, medical consultant, Wallerstein Co., which manufactures both; Dr. Henry Welch, symposium chairman.

Kimble Glass Appoints Fischer & Porter

Fischer & Porter Company, Hatboro, Penna., has been appointed a distributor of the full line of laboratory glassware manufactured by the Kimble Glass Company, a subsidiary of Owens-Illinois. The distributors will carry a complete stock, including Kimax items just introduced and those with the Kimax Teflon stopcock, which is manufactured under license from Fischer & Porter. Many special items of laboratory glass apparatus, including custom glassware, will continue to be manufactured by Fischer & Porter.

Science Teachers Assoc. Presents Atkins Award

Two New Jersey firms, Hoffmann-La Roche, Inc., and Warner-Chilcott Laboratories, have received the Atkins Award presented annually by the New Jersey Science Teachers Association for outstanding assistance in development of more effective classroom science teaching.

New Delaware Packaging Firm

A new packaging firm, Packaging Services, Inc., has been set up in Wilmington, Delaware, for contract flexible film packaging for a highly diversified number of products.

Penick Chicago Branch Celebrates 25th Year

The Chicago branch of S. B. Penick & Company celebrated its 25th anniversary on October 31st with a party attended by present and former members of the staff, a group of more than 50 people.

The branch was established in 1934 by Harold A. Meyer. Since 1946 when Mr. Meyer rejoined the home office in New York, Ralph A. Olson has been in charge of the Chicago operation. Both Mr. Meyer and Mr. Olson are vice-presidents of Penick.

The Chicago branch carries complete stocks of items from all three Penick divisions—Botanical & Allied Products Division, NYQ Chemical Division, and Farm Chemical & Insecticide Division.

Luis de Hoyos (left) general manager, Synfleur Scientific Laboratories, presents pre-Columbian figurine to Governor Rockefeller, the president of New York City's Museum of Primitive Art.

Paul J. Cardinal (left), Hoffmann-La Roche, and Elliott Steinberg, Warner-Lambert, congratulate each other on receiving the Atkins Award for their companies from N.J. Teachers Association.

Snapped at the 25th anniversary celebration of Penick's Chicago branch, Ralph A. Olson (left), who heads it, and Harold A. Mayer, who founded it. Both are vice-presidents of Penick firm.

STOP

AT THE FIRST SIGN OF YELLOW

Look to 2-Amino-2-Methyl-1, 3-Propanediol

White stays white! AMPD soaps are superior in stability of color and in freedom from yellowing or darkening – even after prolonged storage. Neutral soaps of this aminohydroxy compound possess unusually high emulsifying power and have no odor that will interfere with perfuming the final product. Creams made with this compound are remarkably free from oil "leakage". Consistency and texture of creams and lotions remain constant even after long periods.

For cosmetic creams and lotions, brushless shaving creams, hand lotions and mineral oil emulsions, put this superior emulsifying agent in your formula. Write today for samples and technical data sheet. We will be glad to give our recommendations on your particular emulsion problem.

PROPERTIES OF AMPD
(PURE MATERIAL)

Formula	$CH_2OHC(CH_3)NH_2CH_2OH$
Molecular Weight	105.14
Melting Point, °C	109 to 111
Boiling Point, °C	151 to 152 at 10mm
pH of 0.1M Aqueous Solution at 20°C	10.8
Solubility in Water g/100 ml at 20°C	250

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COMMERCIAL SOLVENTS CORPORATION

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Atlanta • Boston • Chicago • Cincinnati • Cleveland • Detroit • Houston • Indianapolis • Kansas City • Los Angeles • Louisville • Memphis • Milwaukee • Minneapolis • Newark • New Orleans • New York • Pittsburgh St. Louis • San Francisco • IN CANADA: McArthur Chemical Co., Montreal • IN MEXICO: Comsolmex, S. A., Mexico 7, D. F.

Sonneborn goes further...

Sonneborn's standards

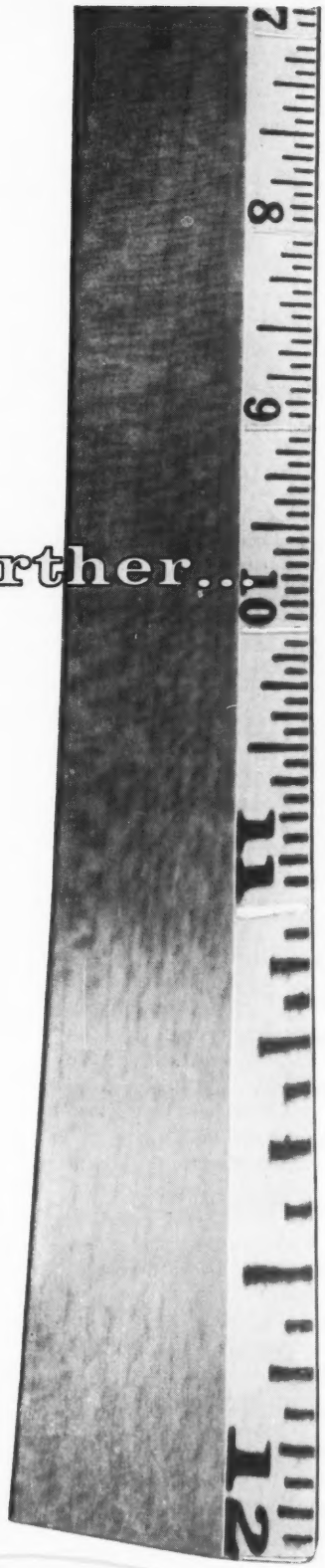
for measuring service

to its customers

are peculiarly its own

There's no rule of thumb at Sonneborn on service. Our degree of specialization in white mineral oils and petrolatum is so great, there can't be. Particularly because the needs of each customer are so different. One asks for a tank wagon overnight; another calls for a special formulation by next week. Still another wants a technician out here "today."

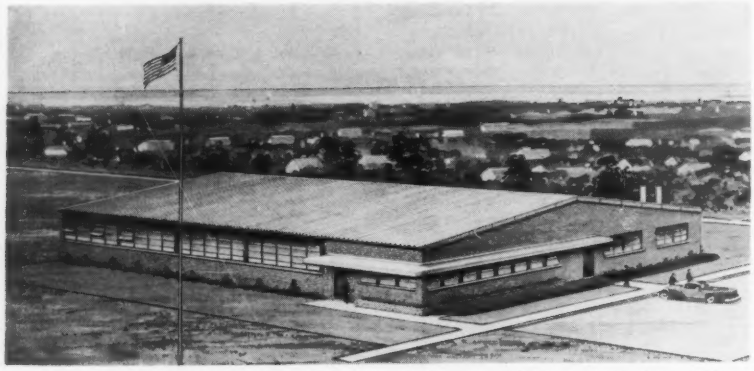
Because we are one of the largest producers of white oil and petrolatum, you expect us to fulfill such requests, and we've been doing it for over 50 years. So we suggest you not only take advantage of our wide range of white oils and petrolatums but also of our specialized know-how in satisfying a customer's needs to the last detail. If you use or contemplate the use of a white oil or a petrolatum, call us in. See why so many customers say—"Sonneborn goes further."



Specialists in
WHITE MINERAL OILS
PETROLATUMS

Sonneborn

L. SONNEBORN SONS, INC., NEW YORK 10, N. Y.



The Arthur Colton Company's new punch and die plant just completed in Elk Rapids, Michigan.

Arthur Colton Completes Michigan Punch and Die Plant

The Arthur Colton Company has completed a new plant in Elk Rapids, Michigan, for manufacturing punches and dies for pharmaceutical, chemical, electronics, and metals industry tablet and compacting presses. All Colton punch and die facilities have been removed from the Mancelona, Michigan, plant to the new facilities in northern Michigan near Traverse City.

The Mancelona plant is now given over exclusively to the manufacture of Colton, Colton-Alpha, and Colton-Hope filling machines.

William Ezra Cornell

William Ezra Cornell, personnel manager of Schering Corporation's Union, New Jersey, plant, died on November 12 of a heart attack. He was 42 years old.

Mr. Cornell has been associated with Schering since 1948.

A great, great-grandson of Ezra Cornell, founder of Cornell University in Ithaca, New York, Mr. Cornell was the only life member of the board of trustees of that University.

Crown Opens Virginia Plant

The Crown Cork & Seal Company recently opened its new can manufacturing plant in Winchester, Virginia, with festivities that included an all-day open house for the public at the plant, and the introduction of Crown's visiting executives and the plant's managing executives to Winchester's business, civic, and government leaders at a luncheon. Visitors attending the festivities were presented with coin banks made from Crown's seamless Spratainers.

William H. Schuette

Dr. William H. Schuette, a vice-president of The Dow Chemical Company and general manager of the Midland Division, died of a heart attack at the Midland Hospital on November 8. He was 47 years old.

Dr. Schuette has been Midland Division general manager since 1955, a director of the company since 1957, and had been elected a vice-president last year. He began with Dow in 1941.

He was a member of the American Institute of Chemical Engineers and the American Chemical Society, among other organizations.

Walter Joseph Murphy

Dr. Walter Joseph Murphy, editor of publications for the American Chemical Society, died November 26 in Georgetown University Hospital, Washington, D. C., after a short illness. He was 60 years old.

Dr. Murphy had been with the Society for 17 years. He also served with other chemical publications.

Edwin J. de Beer

Dr. Edwin J. de Beer, associate research director of Burroughs Wellcome & Co. (U.S.A.) Inc., died on October 27 at Lawrence Hospital, Bronxville, N. Y., at the age of 57.

Dr. de Beer pioneered in the application of statistics to biological experimentation, and was well known for his work on therapeutic agents used in neuromuscular blockade.

He joined the Research Laboratories of Burroughs Wellcome in 1933 after serving for eight years in the Department of Physiological Chemistry at the University of Pennsylvania, becoming acting director of the laboratories in 1946, and associate director and chief of the Division of Pharmacodynamics in 1956.

Dr. de Beer was co-organizer of the Biometric society, now an international organization, and a Fellow of both the American Association for the Advancement of Science and the Royal Society of Tropical Medicine.

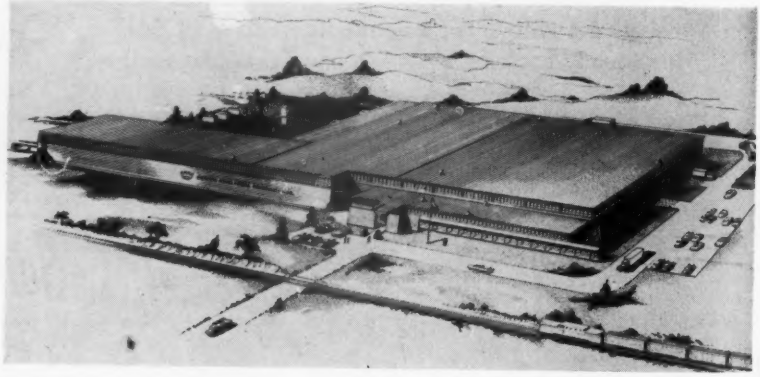
He was also affiliated with the American Society for Pharmacology and Experimental Therapeutics, the American Federation for Clinical Research, and the American Statistical Association.

Arch Payne

Arch Payne, recently elected assistant vice-president of Florasynth Laboratories, Inc., died suddenly on October 29, during a business trip, in Richmond, Virginia. He was 60 years old.

Mr. Payne left the Shell Oil Company 14 years ago to join the Florasynth staff. For the past ten years he has been East Coast sales manager for the firm.

Artist's sketch of the new Winchester, Virginia, can plant of Crown Cork & Seal Company, Inc.



Reheis Chloracel...

basic ingredient for anti-perspirant and deodorant sticks

Available as a 40% w/w solution for making alcohol-sodium stearate sticks, *Chloracel* (sodium aluminum chlorhydroxy lactate complex) is non-destructive to fabrics . . . non-irritating to skin . . . the first material to permit the formulation of anti-perspirant cologne-type sticks.

Write for complete data.

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REHEIS COMPANY, INC.

Berkeley Heights • New Jersey

manufacturers of

Fine Chemicals

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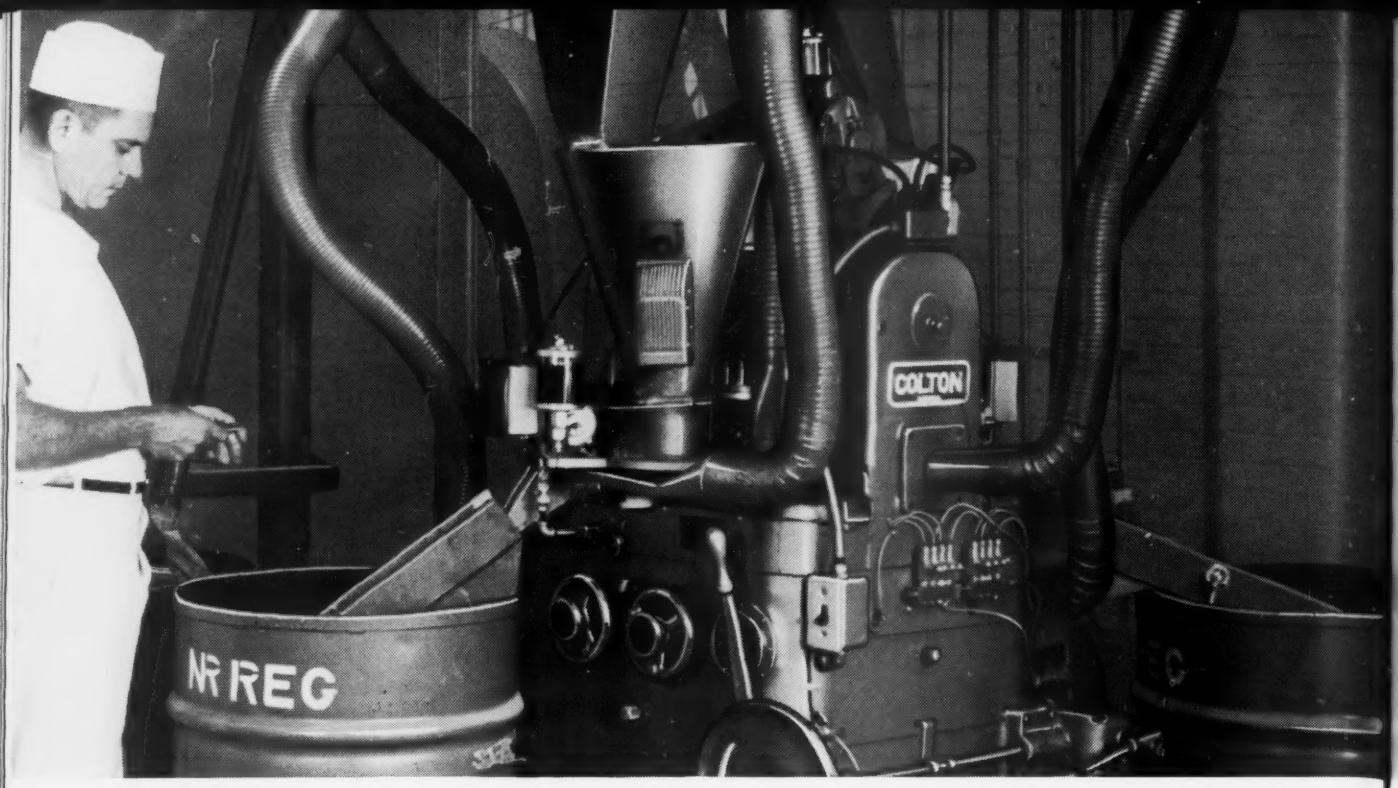

1 COLTON MACHINE

REPLACES 8 ORDINARY MACHINES

AND BOOSTS NR TABLET OUTPUT 70%

Lewis-Howe Company of St. Louis, famous fifty-year-old manufacturer of TUMS and NR TABLETS, has replaced two sluggers, one granulator, five rotary presses with one Colton No. 249 Double Rotary Tablet Press equipped with Colton No. 245 Induced Die Feeders* and thereby raised NR Tablet output from 3,000 to 5,100 per minute, an increase of 70%.

This was possible through the inclusion of Colton No. 245 Induced Die Feeders which provide:

1. Direct tableting of many materials without slugging or granulating and with finer elegance.
2. Uniform density, accurate weight; better disintegration through using powders instead of granules.
3. Positive die fills at higher speeds.
4. Tablet capping and laminating substantially reduced.
5. Practical tableting of 2-layer tablets with minor change-over.
6. Increased production at a fraction of the cost of other equivalent capacity equipment.

In installations such as this there are these collateral gains:

1. Appreciable gain in floor space.
2. A cleaner department because this single Colton press replaces eight machines.
3. Substantial reduction in general area maintenance, mechanical care, power consumption, supervision.
4. Lower operating cost.

We will gladly send you additional information.

*Patents in process. Available on all Colton rotary presses, including those now in use.

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Specialists in Drug, Chemical and Filling Machinery for 75 Years

Management Forum

BY FRANCIS CHILSON
INDUSTRIAL CONSULTANT

Big Companies-Big Blunders

At regular intervals during the life of this column I have inveighed against the industrial colossi, such as the big motor companies, for the reason (among many others) that such corporations can, because of size, make such colossal blunders—the recent announcement by the Ford Motor Company that the Edsel would be abandoned along with the 300-million-dollar investment the company has in this abortion. At the time it was introduced the market and the company did not need another medium-priced car; it already had a good one: the Mercury. The engineering in the Edsel was poor and gave rise to thousands of complaints from those unfortunate enough to fall for the glamorized misrepresentations with which the car was advertised. When one reads the sad history of the Edsel one wonders what was wrong with marketing management that it failed to realize that there was no market for such a car. What was wrong with top administration that it permitted the investment of an immense fortune in a car that didn't have a single extraordinary feature to commend it to the public and thus create its own market? What was wrong with engineering and production management that it permitted so many enginering faults to get by? The answer to all these questions is simply: internal politics. And in this case the Ford stockholders will pay the shot. Such blunders also have an effect on the general economy in lost employment through closed plants, losses to dealers—and the public is stuck with orphan cars.

Multistory Buildings

I have been accused of being fanatically prejudiced in favor of single-story buildings, and the assumption is made that I would never recommend the use of a multistory under any conditions whatever. That, of course, is nonsense. I have revamped a lot of multistory buildings during the past thirty years and these layouts have withstood the test of time and increasing volume. But I did these jobs because there was no alternative in each case. Some companies were all but broke and simply didn't have the money to build new factories. Some, unfortunately, had made enormously costly processing equipment installations that weren't sufficiently depreciated to permit economic removal. Some had local labor and marketing problems that prevented removal. As a rule, I found upon analysis that, with a little imagination and some money for new equipment and material handling devices, capacity could be increased to such an extent that there was no need for removal. In fact, many companies I reorganized and modernized 25 or 30 years ago are still operating in their old multistory buildings and during the interim have expanded sales volume up to 400 per cent. None has been a failure.

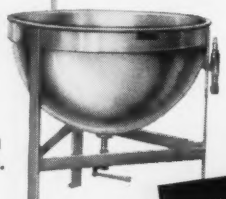
All of which of course does not constitute an argument for a multistory factory structure. Assuming all other factors to be equal, it would be foolhardy to build anything but a single-story structure for factory and laboratory use, especially when there is an opportunity to build in the suburbs or in the country where plenty of inexpensive land is available, particularly for parking. Here's one area where multistory operators are running into serious trouble. Cities, towns and even villages are universally insisting upon off-the-street parking. The multistory structure offers no solution for this problem unless it was specially built to provide for parking on one of its floors like the new apartment houses in New York. Parking is a universal problem which is already critical and will become far worse in the future.

Parking is no problem for a one-story plant located on plenty of land. You need a minimum of land equal to ten times the amount you will utilize initial-

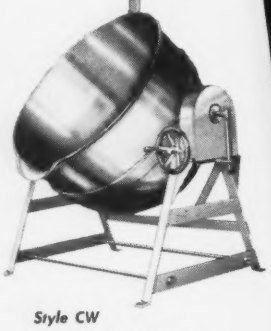
COOKING KETTLES

Style C
Two-thirds Jacketed
5 to 100 gal.

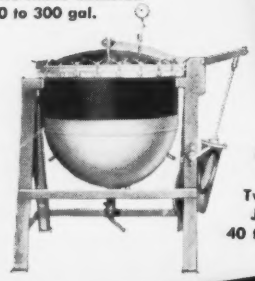
Style A
Two-thirds Jacketed
5 to 500 gal.



Style B
Full Jacketed
10 to 300 gal.



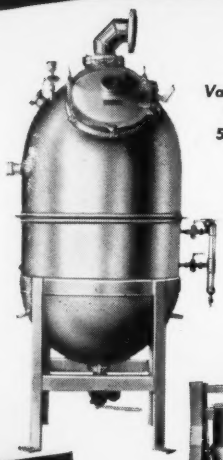
Style CW
Two-thirds Jacketed
80 to 300 gal.



Pressure Kettle
Two-thirds Jacketed
40 to 200 gal.

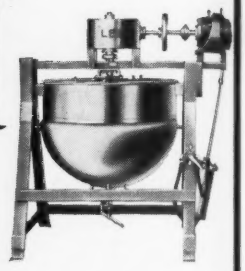
MIXING AND BLENDING UNITS

CW3T
Center-line Scraper Agitator Kettle
80 to 300 gal.

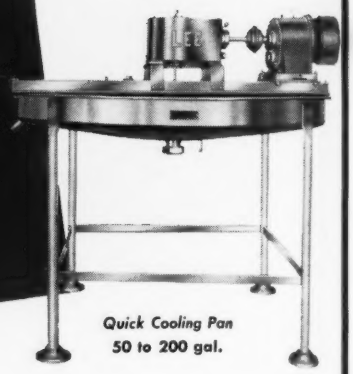


Vacuum Pan
50 to
500 gal.

D3T
Center-line Scraper Agitator Kettle
25 to 300 gal.



these LEE Units WILL REDUCE YOUR PROCESSING COSTS!

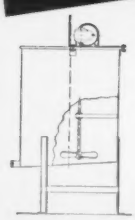


Quick Cooling Pan
50 to 200 gal.

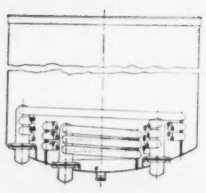
Individually designed for a specific processing operation and available in a wide range of sizes to fit your exacting requirements, Lee corrosion-resistant equipment is built to give you long years of peak performance with minimum maintenance.

Descriptive bulletins are available for any or all of the above units. Write for them today and discover how Lee can help reduce *your* processing costs.

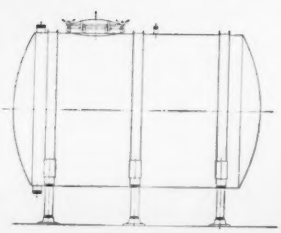
MIXING, COOKING & STORAGE TANKS



Mixing Tank
25 to 500 gal.



Pulp Tank
500 to 2,000 gal.



Storage Tank
100 to 5,000 gal.

LEE METAL PRODUCTS CO., INC.

408 PINE STREET,
PHILIPSBURG, PA.

ALL LEE KETTLES ARE MADE TO A.S.M.E. CODE

ly. It is unsafe to buy less, and if the budget will allow buy land to the maximum available; it is a superlatively good investment.

As I have said so often, all the factors in the single vs. multistory structure can be weighed and a comparison made. The economics are simple. A single-story building is *always* cheaper to build; *always* cheaper to operate. All other factors have to be compared on the basis of simple arithmetic and common sense. While it is true that some companies never have and never will grow out of their present multistory buildings, and—although it is also true that through changes in product mix making possible simpler and possibly automatic equipment—operating space requirements may actually decrease even though dollar volume is increasing substantially, it is nevertheless a fact that sooner or later space for warehousing becomes an acute and costly problem and parking is completely insoluble in the high buildings. Finally the problem must be weighed in the light of our rapidly increasing population and expanding economy. Firms that have good management and reasonably good products should look forward into the long future with great optimism and plan facilities accordingly. Some made the mistake in the past of modernizing facilities that should have been junked and now find themselves in the unhappy position of having to junk inadequate facilities and a very much larger fixed investment than they originally had. One of the numerous virtues of single-story construction is that costly installations such as air conditioning, dehumidification, dust collection, refrigeration, process piping, power and steam distribution mains can be located so that they will never have to be moved until worn out or discontinued for one reason or another.

Industrial Photography

Twenty years ago I stumbled upon the idea of using high-speed photography in machine design. I was working with some other engineers developing a piece of very high-speed equipment. It did its job very well but distorted the product. We spent weeks taking it apart and rechecking all dimensions, curvatures of cams, gear pitches, etc. We were certain something was out of line somewhere but the machine operated so fast that any slight timing differential in any part could not be detected by eye. Then I retained an industrial photographer who made high-speed motion pictures of all critical movements. These pictures were played back in slow motion and in no time we found the fault. I did not know then that industrial photography might have much wider use in factories. I knew of course that films had been used for sales training programs, customer relations and dealer programs, but the field was limited especially in our industry. But a number of firms are now using films for training factory employees. Kodak has reported that a great many of the large firms have their own photographic laboratories as adjuncts to their research and engineering departments.

English Factory Reports

I got a letter recently from R. B. Seymour, Director of Manufacture for the new Aspro-Nicholas plant at Slough in England, which tickled me pink, as they say in Australia. Dick reports that during the past year some 900 visitors have seen the plant and commented voluntarily that it was the cleanest and most efficient plant they had ever seen. A good many of the visitors were from the States too. I am sure you too would say the same thing. You could count the plants in the U. S. that can come anywhere near matching it in any respect on the fingers of one hand. What interested me particularly was that a majority of the visitors commented upon the apparent good fellowship that exists among the Aspro personnel. This is one important result of efficiency, cleanliness, and attractiveness in plant operations and environment which is insufficiently commented upon. Dick Seymour was my engineering colleague during the design and construction of the plant and, as reported recently in this journal, he assumed control of operations when the plant was finished and operating. He has a fine, efficient, and intelligent group of men assisting him in the operation of the plant.

Government Control of Research

While I am naturally an optimist about the future of our country, it worries me when more than half our national budget is spent for military purposes and that that portion of our budget, necessarily government-controlled, is now so necessary to the maintenance of our expanding economy that business men, eager for profits and full employment, are willing to accept government control—in other words a planned economy—to this extent without thinking of the totalitarian implications in all this. Also the government is stepping into controlled research. It is this possibility that worries me more than the first. I would like to quote a few trenchant paragraphs from Richard LaPierce's recent book *The Freudian Ethic*.

"For the most part, additions to scientific knowledge have come from those traditional citadels of freedom from practical concerns and social constraints—the universities. During the Middle Ages the universities were very loosely organized islands of free inquiry in a sea of theological authoritarianism. They may at times have produced nothing but random discourse on unimportant matters; but they developed and maintained the concept of free inquiry, and they transmitted this as an ideal to successive generations of students, some few of whom abandoned philosophical speculation in favor of scientific discovery. Such discovery requires not only

3 ways to PRECISION LABELING

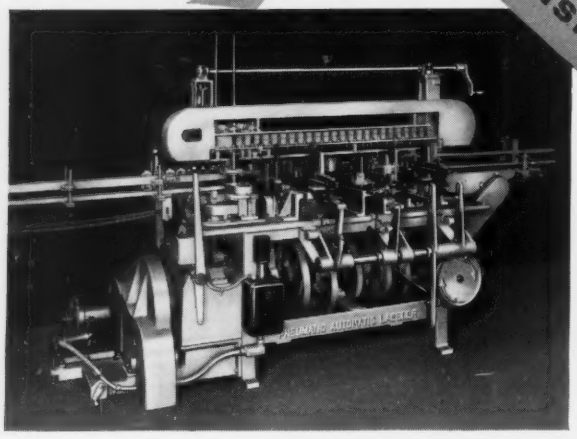
COLLETTA

McDONALD

DIREC-TRANSFER

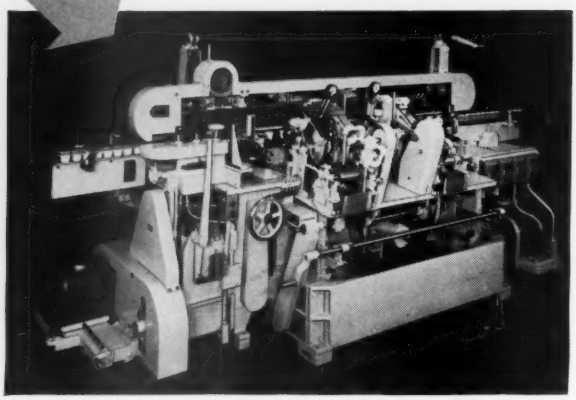
Portable bench type labeler for convenient application to wide range of shapes in glass, boxes, cartons, books and other objects. Offers full-surface gluing for high quality results. Changing from one job to another is a simple procedure, taking a maximum of five minutes.

Basically a semi-automatic unit, this model is easily made automatic by the use of available auxiliary attachments. Designed by Jagenberg of Dusseldorf, this precision built labeler is sold exclusively in the United States by Pneumatic.



This 4" Simplex unit is one of several models offered by Pneumatic as standard labeling equipment for over thirty years. Using 'glue on bottle' method for label pick-off, the McDonald Labeler has proved its efficiency in literally hundreds of installations. All models are well equipped with safety devices to prevent loss of production time and materials. Round, oval or rectangular shapes may be run with front only or both front and back labels being applied simultaneously.

PNEUMATIC SCALE CORPORATION, LTD., 70 Newport Avenue, Quincy 71, Mass. *Sales Offices: New York; Chicago; Dallas; Rochester. Agents: Fred Todt Company, Los Angeles, San Francisco and Seattle; Rockwell Pneumatic Scale Ltd., London N. W. 2, England; O. R. M. A. Paris, France. Subsidiaries: Delamere & Williams Co., Ltd., Toronto; Carbert Manufacturing Co., Inc., Cambridge, Mass.*



Duplex in action, this Labeler handles two containers at a time for front only or both front and back application. A three-station indexing turret with suction pads picks labels off bottom of label stack as turret revolves in counter-clockwise direction. Each label receives thin, uniform coating of adhesive from roller and is given time to "temper" as it travels to next station. At final position of turret, the label is transferred directly, through contact, to bottle. Continuous straight-through intake provides gentle handling of glassware, and bottles are in positive control throughout labeling process. Equipment includes "no bottle, no label" and "no label, no glue" safeties.

★PNEUMATIC *Packaging and Bottling Equipment*

individual initiative but a reasonable degree of freedom for the scientist to pursue his own interests, however futile they may seem to others.

"General acceptance of the scientist as a potential social asset was long delayed. Indeed, he was often scoffed at and sometimes even stoned. For the past century or so, however, 'science' has become synonymous with 'progress.' It seems odd, therefore, that no very important new provisions have been made for the perpetuation of scientific endeavor. The technician's need for new scientific knowledge is rapidly increasing, and the problems of the scientists are becoming ever more complex. But even the university, though still the pirmary center of scientific work, has of recent years lost some of its traditional freedom to subsidize and otherwise encourage scientific endeavor.

"The recent development of governmentally sponsored contract research has accelerated the trend toward large-scale, highly organized research projects in the universities. On the whole, those university scientists who have become involved in contract research have been lost to pure science. Many of them, in fact, have found themselves—pleasantly and profitably, perhaps—removed from research entirely. The military contracts are invariably big operations, and under them research is programmed. This means, in the first instance, that the research process is largely planned in advance and that the actual work is done by a large number of men, each assigned some special and limited task. It also means that the scientist who accepts responsibility for such a project inevitably becomes the administrator of a complex bureaucratic organization, whereupon he ceases to be a research scientist and is reduced to the role of a research entrepreneur."

A very high government official told me recently that controlled research is necessary in order to match the Russians and produce a totally invulnerable offensive and defensive force. But if government increases its control of research and eventually of industry, what's the point of trying to match or beat the Russians? Our system will have become as totalitarian as theirs.

Depressed Areas

In this country we have a few depressed areas where local resources such as coal have petered out, or where industry shifts have eliminated the livlihood of single-industry towns. Scranton, Pa., and Lowell, Mass., are typical examples. When a town begins to wither as an industrial center, it is not possible for the entire population to pack up and shift to another location. Too many small businesses have been established to service the local population and too many social ties have been created in the community to be easily broken.

State and Federal governments could stop the slow death of dying towns by providing income and other tax relief for definite periods to companies willing to establish plants in such areas. The amount of relief given could be based upon the number of people employed. Both Federal and State governments could do much to attract and stimulate new businesses by suspending all income taxes on new companies started in depressed areas and on small companies moving to such areas. In time—perhaps a century—all industrial towns may have become sufficiently diversified so that the loss of a single business will not throw the local economy out of gear.

Process Industries Equipment

Equipment, systems, and controls for the process industries are featured in a new bulletin, B-I-F 5-1, recently issued by B-I-F Industries, Inc., 345 Harris Ave., Providence 1, Rhode Island. Representative equipment from Builders-Providence, Proportioneers, and Omega divisions of the company is included.

The eight-page bulletin in two colors contains information on flow meters; process instrumentation (transmitters, receivers, miniature instrumentation); feeders for solids and liquids; feeding systems; and blenders, additive systems and process equipment.

Rotary Fillers

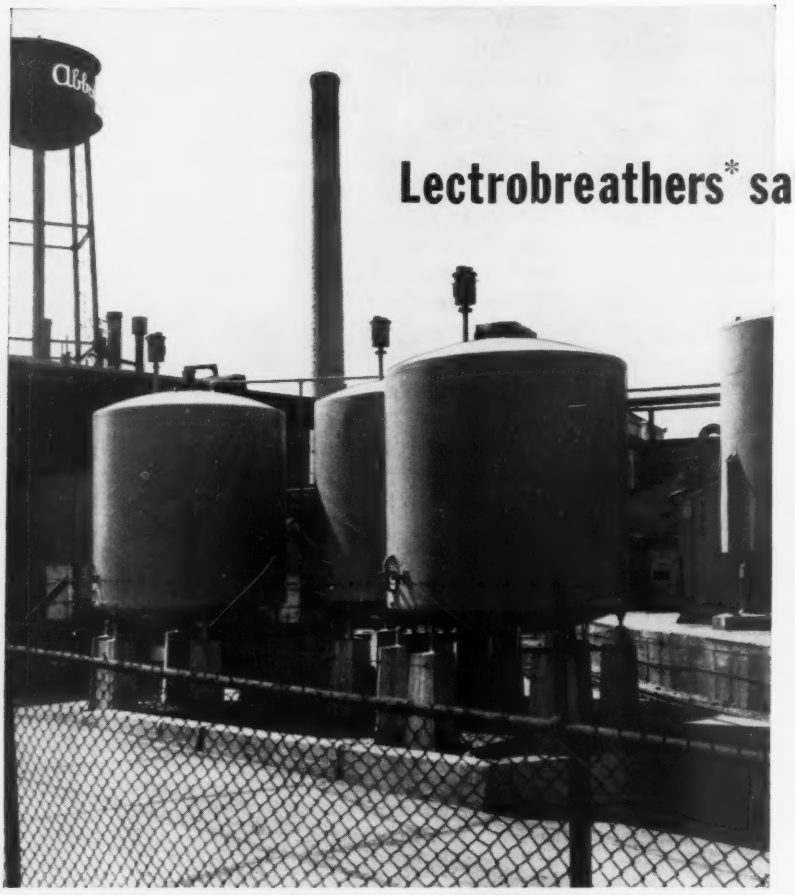
The Karl Keifer Machine Company, 924 Martin Street, Cincinnati 2, Ohio, has announced a new No. 5 Series of Rotary Vacuum and Rotary Pressure-Vacuum Fillers. The machines in this series are built with either 24, 36, or 48 filling stems, and can fill from a fraction of an ounce to 10 quarts.

Many new features of the line include: gradual acceleration in starting and rapid deceleration in stopping; safe and sensitive lifting of container trays, which prevents damage to filling stems; an automatic liquid flow control assuring optimum supply for any filling speed; safety detents in the container-handling system, which prevent breakage of glassware; a new device for elevating and lowering head, making for fast predetermined container-height change; construction allowing rapid disassembling for thorough cleaning; and automatic lubrication to all bearings and moving parts.

Automatic Frost Preventor

Niagara Blower Company, 405 Lexington Avenue, New York 17, N. Y., has developed an automatic apparatus for preventing frost accumulation on the refrigerated coils of large-scale commercial freezing and cold-storage installations, with convenient disposal of the condensed moisture.

A nonfreezing, hygroscopic liquid is sprayed over the cold coils of a fan cooler, absorbing the moisture as fast as the coins condense it. As this condensate water dilutes the absorbent solution to the point where freezing becomes possible, its strength is restored by the Niagara No-Frost Concentrator. The Concentrator adapts a submerged electric water



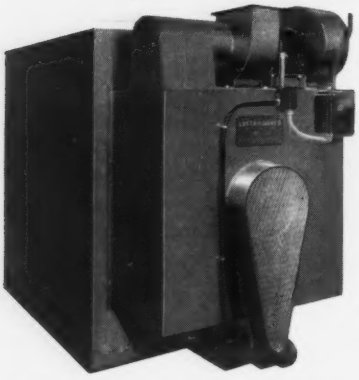
You see Lectrobreathers extending above tanks and rooftops at the Abbott Laboratories plant in North Chicago, Illinois.

Lectrobreathers* safeguard chemicals in storage—permitting carload purchases

● Buying liquids in tank car lots saves money. But profits are quickly washed out if storage tanks are allowed to inhale wet air as they breathe, contaminating their contents.

Abbott Laboratories solved this problem by installing Lectrobreathers on many of their outdoor and indoor storage tanks. Now, as pressures vary and those tanks draw in outside air, that air is DRY. The original high quality of their contents is preserved.

Lectrobreathers and Lectrodryers make certain that any tank, little or big, breathes only DRY air. For help in selecting the equipment you need, write Pittsburgh Lectrodryer Division, McGraw-Edison Company, 309 32nd Street, Pittsburgh 30, Pennsylvania.



Where volumes of air are large, as in a tank farm, a Lectrodryer serves as a breather. Its DRYing-reactivation cycle is continual, so it stays right on the job.*

◀ *A tank breathes freely as air passes through the Activated Alumina adsorbent and is dried DRY. When a Lectrobreather needs reactivation, it is lifted off and a spare takes its place.*

McGRAW EDISON

Lectrodryer

*REGISTERED TRADEMARK U. S. PAT. OFF.

heater to provide sufficient heat to evaporate the water while the reconcentrated liquid is returned to frost prevention.

The concentrator operates thus: the dilute solution first passes through a heat exchanger to interchange its heat with that of the returning concentrate. It is heated by a hot-water coil to about 140° F. maximum in the spray pan and is then sprayed in an air stream which evaporates and removes the water. The concentrate, separated from the water vapor by an air-to-air reflux cooler, flows back to the refrigerating unit.

The equipment avoids fire hazards, is easy to keep clean and reduces the chance of operational failure. It comes in four sizes, with a capacity range sufficient for the largest tonnage refrigeration systems.

Bottom Filling Attachment

The National Instrument Company, Inc., Baltimore, Maryland, has introduced a Bottom Filling Attachment that adapts Filamatic portable fillers for filling foaming liquids. With this attachment, filling nozzles are automatically lowered into the bottles and then raised as the liquid level rises in the container. An adjustment permits the rate of rise to be regulated to coincide with the speed at which the bottles are being filled, eliminating or minimizing foaming and permitting faster filling speeds.

An adjustable nesting jig adapts the Bottom Filling Attachment for use with containers of any size up to 16 ounces. The rate of rise of the nozzles is regulated by an electronically controlled, variable-speed motor connected to a uniform-motion can.

The attachment can be factory-installed on any dual type Filamatic liquid filler.

Tablet Inspector

Popper & Sons, Inc., 300 Fourth Avenue, New York 10, N. Y., has announced the Model TL-6 Tablet Inspector, which permits a single operator to make a thorough inspection on both sides of tablets and capsules. Rates of 50,000 to 150,000 units per hour can be achieved, and rejects can be removed either manually, or by vacuum pickoff.

Simple design facilitates changeover from one shape or size of tablet or capsule to another. Extra sets of perforated chip and powder removal plates are available for various sizes of tablets. A large capacity hopper allows long, uninterrupted inspection periods.

Popper has also announced its Model GA-6 Label Paster, a multi-purpose machine for efficient labeling in all packaging departments. Unique key-in-groove coupling permits greater ease of cleaning than has been possible before—there are no belts or pulleys. It is simply designed for mobility and trouble-free service.

Another new development is a line of high-speed piston fillers. The nine different versions handle glass and plastic containers from one dram to 32 ounces in capacity, at rates of from 3,000 to 15,000 per hour.

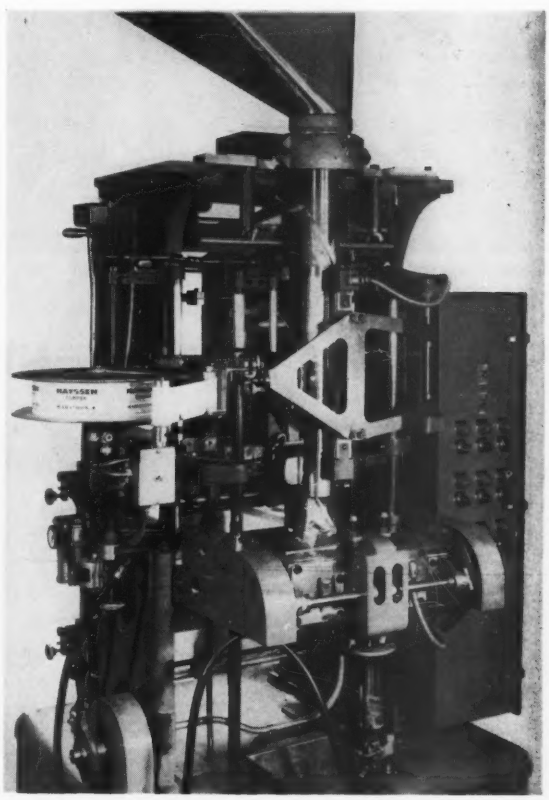
Heavy-Duty Dissolver

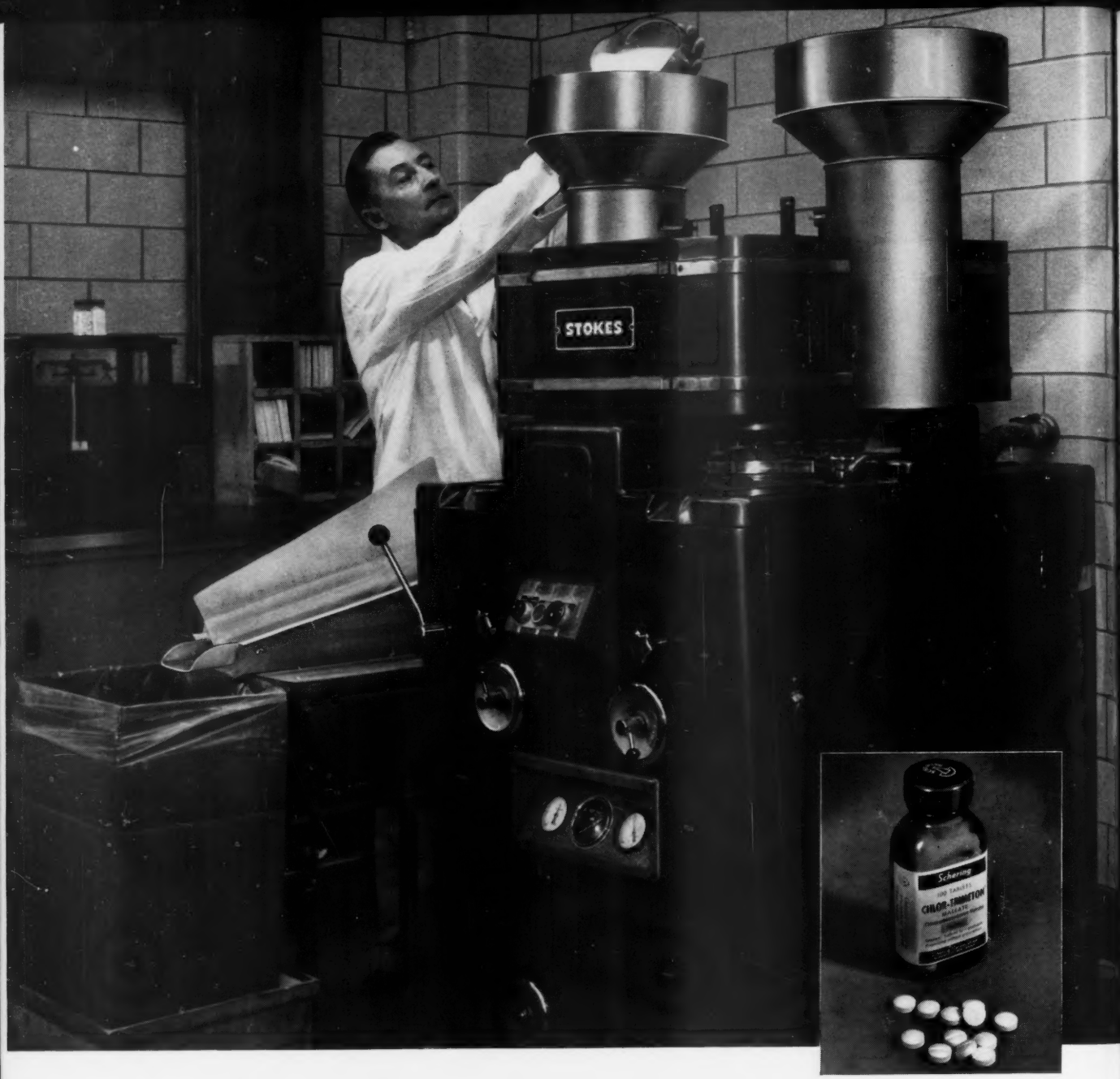
The J. H. Day Company, division of The Cleveland Automatic Machine Company, 4932 Beech Street, Cincinnati 12, Ohio, has added to its line of processing machinery a heavy-duty dissolver for mixing extra-viscous solutions. Called the Daysolver, it is built with a heavy-duty steel column, frame, and bridge, with oversize stainless steel impeller shaft, to provide smooth, vibrationless operation under extreme work loads.

The bridge swings in a 240° arc, which makes it possible to mix one batch, with other drums of material positioned along the arc of swing ready for mixing, thus making for practically continuous operation. A special locking device is contained within the column for positive locking of the arm.

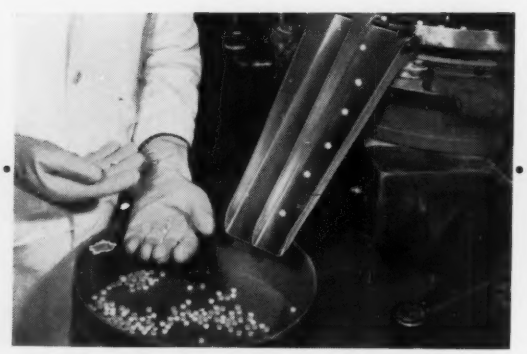
Automatic Labeling Attachment

The Hayssen Manufacturing Company, Sheboygan, Wisconsin, has introduced a header label attachment for its Compak automatic packaging machines, which automatically applies a label to the forming package while it cuts it from roll stock. The label is finish-sealed as the package is sealed. The attachment works at the speed of the machine and eliminates the services of at least two persons required for semi-automatic labeling systems.





OTHER STOKES EQUIPMENT AT WORK FOR SCHERING . . .



Schering uses a Stokes 566 Multi-layer Tabletting Machine for perfection in multi-layer tablets. Stokes exclusive layer pre-compression permits periodic weight checks—gives clean, sharp separations.

Part of a bank of Stokes Polishing and Coating Pans at Schering. Here, standard Stokes machines have been neatly built into a custom installation behind gleaming stainless steel panels fitted with glass doors.

Operator Kenneth W. Shaw fills the hopper of one of the Stokes high speed Model 540's at Schering. This 41 station machine produces many Schering products, such as Chlor-Trimeton-Maleate, at rates in the order of 3000 tablets per minute.

Accuracy is important and is checked often at Schering. The centralized control area provides constant visual indication of speed and pressure at the punches. Single hydraulic release control permits absolute tablet uniformity from both compression stations of the double sided Model 540.

Dependable high-speed production for Schering...with Stokes pharmaceutical equipment

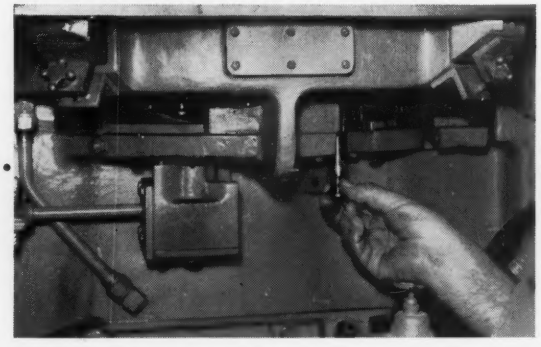
Schering Corporation, Union, New Jersey, demands maximum reliability, efficiency and speed in producing their broad line of steroid hormones and other pharmaceutical products—both ethical and over-the-counter.

Schering's tabletting operation depends on Stokes equipment. Most recently installed are two Model 540 Rotary Tabletting Machines that are in constant operation 16 hours a day, 5 and 6 days a week, manufacturing a variety of drug products. Chlor-Trimeton-Maleate anti-histamine and anti-allergic formula, for example, is produced at speeds up to 3000 per minute. These tablets are 200 mg., imprinted and scored. The high speed and dependability of this operation keeps tabletting costs at their lowest possible level.

Schering takes advantage of the complete line of Stokes pharmaceutical equipment. In addition to operating many Stokes tabletting machines—including conventional and multi-layer—Schering processes their products in Stokes mixers, oscillating granulators, coating pans and polishing heads. And, of course, Schering uses long lived Stokes punches and dies in their tabletting machines.

Find out how this advanced design pharmaceutical equipment can save on your own production. Write to Stokes for complete information, or call your nearest Stokes office.

Pharmaceutical Equipment Division
F. J. STOKES CORPORATION
5500 Tabor Road, Philadelphia 20, Pa.



Maintenance problems are small at Schering. Here, the photographer caught the operator changing punches—snapped this picture because it illustrates the ease with which such service is accomplished on the Model 540.

STOKES

Season's Greetings —by the Tons

- Our sincerest thanks for the privilege of serving you
- Our best wishes for a very successful and prosperous New Year

FROM THE
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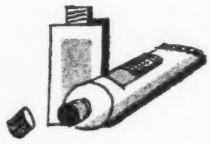
in the United States and Canada
and our distributors



Advancing Therapy

New Diuretic

As another variation on the chlorothiazide theme, the SO_2 group in the benzothiadiazine 1,1-dioxide has now been replaced by the CO group, with apparently little or no loss of diuretic activity. E. Cohen, B. Klarberg, and J. R. Vaughan, Jr., of Lederle report in *J.A.C.S.* 81: 5508, 1959 that 7-chloro-6-sulfamyl-4(3H)-quinazolinone, an analog of chlorothiazide, and 7-chloro-6-sulfamyl-1,2,3,4-tetrahydro-4-quinazolinone, corresponding to hydrochlorothiazide, caused marked natriuresis and chloruresis in rats and dogs with only slight increase of potassium excretion. The second compound is the more active, with less potassium excretion.

Comment: We can confidently expect that the corresponding compounds with CF_3 replacing the chlorine atom will be made, for the customary permutations, once useful activity has been related to a chemical structure.

Iproniazid in Angina

The results obtained during the double-blind study reported by M. Shoshkes et al (Circulation 20: 17, 1959) demonstrated that iproniazid at the recommended dose level of no more than 50 mg/day can be very helpful in relieving the pain in patients who have ischmic heart disease with the anginal syndrome. The percentage of relief of symptoms was as high in this study as in studies previously reported in which 150 mg/day was used. The demonstration of a gradual accumulation of pharmacologic effect emphasized the need for patience in awaiting the desired response. The authors believe that, except for a possible specific hepatotoxicity, the reported side effects of iproniazid are manifestations of overdosage. Iproniazid proved effective in relieving the pains of 64 per cent and 73 per cent of the patients during 2 separate periods, whereas the placebos were effective in only 30 per cent of the patients during 2 separate periods; these differences were statistically significant. The effects of iproniazid were slowly cumulative, as demonstrated by an increasing rate with time of both therapeutic effectiveness and of untoward reactions. At the dosage level used, iproniazid produced a mild hypotensive effect and an elevation of mood and aided in maintaining body weight. There was no alteration in the clinical course or in the progression of the primary heart disease.

Alimemazine Tartrate

Almemazine tartrate, an amino derivative of phenothiazine, is a powerful neuroleptic acting upon the central nervous system. Its empirical formula is $(C_{18}H_{22}H_2S)_2$, $C_4H_6O_6$. Its sedative properties make it valuable for use in psychiatric therapy. Fifty women who had had psychiatric illnesses for a long time, and who had had other treatment which was not successful, were given alimemazine tartrate in progressively increasing doses by A. F. Zoila, J. Basset and M. Lebreton (Presse Med. 67: 935, 1959). The muscular relaxation obtained assured a good emotional readjustment with agreeable behavioral changes. The sedative action on the central nervous system assured regular nocturnal sleep unperturbed by extrapyramidal muscular hypertonicity, without marked somnolence during the day. The authors observed an antidepressive and hallucinolytic action with controlled euphoria and better social adjustment. The usual inconveniences associated with treatment by chlorpromazine and reserpine were not observed. The only examples of intolerance were some lipothymic tendencies without a lowering of blood pressure in older patients and 2 paroxysmal epilepsies in patients with progressive organic disease.

Tolbutamide Failure

Euglycemic effects of treatment with sulfonylurea derivatives can be anticipated in 70 to 90 per cent of those mature diabetic patients in whom ketotic tendencies are absent. The 10 to 30 per cent of cases in which a normoglycemic response is not obtained from such therapy are referred to as primary failures. Of increasing importance is a group of patients who respond well for more than one month and then become nonresponsive even though the dose is increased. Such secondary failure of response occurs without infection, weight gain, or other apparent cause; it has been reported to occur in 3 to 33 per cent of patients treated with sulfonylurea drugs. The most likely explanation of this phenomenon is that secondary failure of response to these drugs is a manifestation of the progressive course of the disease, such as is observed in patients treated by other methods. It has been suggested that exhaustion of the beta cells of the pancreas may be responsible, but experimental proof in animals is lacking. A less likely explanation is that of "tachyphylaxis," i. e., the formation of antibodies to the sulfonylurea drugs.

The significant findings of a follow-up study by De W. E. De Lawter et al (*J.A.M.A.* 171:1786, 1959) of nonketotic diabetic patients treated with tolbutamide are: 1. In a group of 200 patients who received tolbutamide and were followed up for up to three years the rate of sec-

ondary failure of response to the drug was 29.5 per cent. In the first year the rate of failure in the same group of patients had been 16 per cent. The monthly rate of secondary failure averages about 3 per cent of the patients treated each month. If this rate continues, all patients will eventually become resistant to the hypoglycemic effects of tolbutamide. 2. Patients with poor and fair initial diabetic control develop secondary failure sooner than those with good and excellent control. 3. There was no significant change in the insulin requirements of patients before treatment with tolbutamide and after their secondary failure of response to the drug. 4. Only 2 of the 25 patients who were given a retrial on tolbutamide therapy obtained a good response. Therefore, it can be anticipated that once a patient fails to respond to the drug the failure will be permanent. 5. A satisfactory response to treatment with chlorpropamide or metahexamide was obtained in 20 per cent of the patients in whom secondary failure of response to tolbutamide had occurred. Phenethylbiguanide gave a satisfactory response in 55 per cent of these. 6. All mature, nonketotic diabetics whose condition cannot be controlled by diet alone deserve a trial on tolbutamide therapy. 7. These patients must be followed up at least every two months, because they may develop secondary failure with little warning and no apparent cause.

Cytoxan

A new chemotherapeutic agent that has shown useful qualities in palliative treatment of certain types of cancer has just been announced by Mead Johnson & Company. It is called Cytoxan.

A potent cytotoxic agent, Cytoxan is the result of extensive research by many investigators to develop an agent with more effectiveness and lower toxicity than nitrogen mustard.

Two of the outstanding features of the new agent are that it appears to be better tolerated than nitrogen mustard, and that it causes less prolonged depression of the white blood cell count.

The new drug, whose generic name is cyclophosphamide, was originally synthesized in Europe by Asta-Werke A. G., Brackwede, West Germany, and has been extensively tested in the United States.

Experience with more than 500 patients in U. S. clinical trials, as well as extensive earlier trials in Germany, indicate that Cytoxan is particularly valuable for treatment of certain malignant neoplasms, especially those arising from the reticuloendothelial and hematopoietic systems as well as certain "solid tumors." It possesses the distinguishing characteristics of wide therapeutic range, high therapeutic index, and low toxicity.

Cytoxan is not a cure for cancer nor is it equally effective in all types of cancer. But, with proper use in specific indications, it may produce remissions of varying duration. In those cases where it is effective, Cytoxan may produce regression of tumor size, relief from pain and other symptoms, increased appetite and increased functional capacity.

Chemically, Cytoxan is a cyclic phosphamide ester of nitrogen mustard. Its exact mechanism of action, like that of other alkylating agents, is still uncertain and the subject of extensive research efforts.

Though systemic side effects and local side reactions are considerably minimized in comparison with nitrogen mustard, Cytoxan often produces nausea and vomiting, depending on dose and individual susceptibility. Temporary alopecia has occurred in 28 per cent of the cases in one series, but hair returned when therapy was discontinued or dosage reduced. Leukopenia is an expected effect.

Among the 500 or more clinical cases already reported were 95 treated by Drs. Coggins, Ravdin and Eisman at the University of Pennsylvania. These investigators concluded: "Objective regression in approximately one-third of (evaluable) patients treated suggests that this agent is more effective than the present standard alkylating agents in use." They noted also that pain relief, in the sense that narcotics could be discontinued or reduced to negligible quantities, occurred in 70 per cent of patients having this symptom at onset of therapy.

In a tabulation of 350 clinical cases the following malignancies had these percentages of positive response (excellent, good, fair or transient): Hodgkin's disease, 71 per cent; lymphosarcoma, 68.4 per cent; giant follicular lymphoma and other lymphomas, 100 per cent; reticulum cell sarcoma, 81.8 per cent; chronic granulocytic leukemia, 100 per cent; mycosis fungoides, 100 per cent. On the other hand, these less susceptible neoplasms had the following percentages of response: carcinoma of cervix, 5 per cent; carcinomas of stomach and of bile ducts, 0 per cent; carcinoma of pancreas, 17 per cent; carcinoma of breast, 25 per cent; malignant neoplasm of the bladder and carcinoma of thyroid, 0 per cent.

Phenyramidol

Experimental studies in animals demonstrated that phenyramidol hydrochloride [2-(β-hydrooxypenethylamino)-pyridine hydrochloride] was a relatively non-toxic compound with two primary pharacological actions. It produced both analgesic and muscle relaxant (interneuronal blocking) effects after either parenteral or oral administration of doses far below toxic levels.

The analgesic activity of phenyramidol was evaluated by various methods and the results obtained were compared with those found using codeine, d-propoxyphene, carisoprodol and aspirin. Analysis of the results indicated that, in animals, the analgesic activity of phenyramidol was comparable to codeine and consistently superior to d-propoxyphene, carisoprodol and aspirin.

The muscle relaxant effects of this drug were evaluated by several methods involving both specific and non-specific testing procedures. Drugs tested for comparison were mephenesin, meprobamate and carisoprodol. Specific evidence of the interneuronal blocking action of phenyramidol was obtained by determining its effects on the flexor and linguo-mandibular reflexes in decerebrate dogs. Results obtained using other, less specific procedures (such as loss of righting reflex, slide from an inclined screen and effects in several unanesthetized animal species) also showed the muscle relaxant effects of phenyramidol. When compared with the other drugs tested, phenyramidol proved to be the most active interneuronal blocking agent.

T. B. O'Dell, N. Y. Acad. Sci. conference on relief of pain, Dec. 4, 1959.

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DRUG & COSMETIC CATALOG 1960-61 EDITION

The only comprehensive reference book published biennially exclusively for the Drug & Cosmetic Manufacturers over the past 29 years. New edition will be published in the spring of 1960.

What's in it?

Alphabetic lists in separate sections giving SOURCES OF SUPPLY FOR ALL RAW MATERIALS, MACHINERY, PACKAGES AND PACKAGING MATERIALS USED BY OUR INTER-RELATED FIELDS.

AEROSOL SECTION listing all contract fillers and sources of supply for all ingredients and machinery for the production of Aerosol packages.

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A list of all PRIVATE FORMULA houses.

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Compounder's Corner

Humectant Action

The influence of humectants on the properties of a vanishing-type cream was considered by D. M. Bryce and J. K. Sugden (*Pharm. Journal*, p. 311, November 14, 1959) with respect to effect on bulk physical properties. Glycerin, propylene glycol, 70 per cent sorbitol syrup and polyethylene glycol in various concentrations were incorporated in a vanishing cream made from 22.0 stearic acid, 1.0 triethanolamine, 0.2 per cent methyl paraben, and water to make 100.0. The cream was made by melting the stearic acid at 75° C. and adding the preservative; triethanolamine was dissolved in the water at 70°. The aqueous solution was added to the fatty acid and mixed with a spatula; water was added to replace evaporation loss. Humectants were added to the aqueous phase, replacing an equal weight of water. Creams were made with 1, 2, 4, 8, 16, and 32 per cent of each humectant. Samples of each cream were packed into a polystyrene jar, 5 cm. in diameter and 3 cm. deep and levelled with a spatula and allowed to stand at room temperature and relative humidity, about 21 to 24° C. and 45 to 65 per cent R.H. Jars were weighed just after filling, twice daily for two days, then daily until the fourth day, and then every other day for a total of 13 days.

All concentrations of glycerin had some ability to retain water, but the 1 per cent cream produced an effect that was exceeded only in creams containing 16 and 32 per cent. Creams containing propylene glycol showed a similar pattern. In the case of the polyethylene glycol 400 creams, the 8 and 2 per cent creams lost more water than the control in four days, losses from the 1 and 16 per cent creams being less. Creams containing sorbitol showed least water loss at 32 and 16 per cent concentrations, next best at 1 per cent, followed by the 8 per cent cream. Water losses from the 4 and 2 per cent creams were greater than from the control. Pearliness was generally greater in creams with higher percentages of the humectant; crust formation was less marked with more of the humectant. Gloss of the freshly cut surface did not seem to be related to humectant type of concentration.

In all the creams, the effect of 1 per cent humectant was quite marked. At higher concentrations, there may be modification of the emulsifier system, as indicated by modification of the triethanolamine stearate cooling curves.

The authors draw the following conclusions: the addition of a polyol to an emulsion may markedly affect its properties; there appears to be a critical concentration of humectant beyond which water-retention decreases until very large amounts are added; crust formation is reduced by a humectant.

Ion Exchange Resins

The November 1959 issue of the Rohm & Haas "Amber-Hi-Lites," No. 54, lists and describes the company's "Amberlite" ion exchange resins in compact tabular form.

There are four major groups of resins: strongly acidic resins containing sulfonic acid groups; weakly acidic resins containing carboxylic acid groups; strongly basic resins containing quaternary ammonium groups; weakly basic resins containing a mixture of primary, secondary, and teriary amine groups. Weakly acidic and basic resins can only exchange ions or absorb acids and bases, but cannot split salts. Strongly acidic and strongly basic resins undergo the same exchange reactions as the weaker resins, but also have the ability to split salts. Most of these exchangers are available in the 16 to 50 mesh technical grade for industrial use. Nuclear and Analytical Grade resins are chemically purified for their special purposes.

Refined grades of resins are available in very small particle sizes for chromatography and research in food, pharmaceuticals, biochemistry, and organic synthesis. These resins have been found to be excellent carriers of drugs for flavor masking or prolonged release.

Liquid "Amberlite" ion exchangers are a recent innovation. They undergo the same ion exchange reactions as the conventional resins but can be used more readily in continuous ion exchange techniques where use is made of their water insolubility and solubility in solvents for liquid-liquid extractions.

Artificial Suntan

We have not had a chance to explore the subject as much as we'd like to, but there seems to be a great deal of interest in the product Man-Tan, a transparent pale green alcoholic solution to be applied daily to the skin to develop a gradually deepening color simulating a natural suntan. According to a story in "Chemical Week," December 5, the product is reported to contain dihydroxyacetone, alcohol, and water, along with the vitamin D claimed on the label. A test on the arm showed that the product did indeed produce a gradually developing yellow brown stain. All we have been able to determine from the literature at hand is that dihydroxyacetone, $CH_2OHCOCH_2OH$, is a compound that readily forms an equilibrium mixture with glyceraldehyde, CH_2OHCH_2OHCHO, and is probably

oxidized by air to caramel-related polymer with a yellow-brown color.

Emollient Ointment

L. F. Tice and M. Barr of the Philadelphia College of Pharmacy and Science discuss a water-in-oil emollient cream for inclusion in the next U. S. Pharmacopeia in the "Practical Pharmacy Edition" of the "Journal of the American Pharmaceutical Association," vol. 20, p. 665, 1959. The structure of the epidermis and specifically those portions involved in dry skin was discussed, along with factors involved in the etiology and treatment of excessively dry or chapped skin. Two formulas, for an oil-in-water cream and for a water-in-oil emulsion were presented and discussed.

In approaching this problem, the authors were immediately faced with the problem as to whether a therapeutically useful emollient ointment should be simply of an oleaginous composition or an emulsion. If an emulsion were selected, it would be then necessary to decide whether it should be a water-in-oil (W/O) or an oil-in-water (O/W) system. Emulsion products are much more acceptable by most patients and they are more elegant from both the pharmaceutical and cosmetic standpoints.

An emulsion, furthermore, provides an opportunity for bringing some water immediately in contact with a dry skin helping in its initial softening. A W/O emulsion theoretically would be expected to be much more occlusive in its action than would an O/W preparation and, therefore, a better emollient. There is the further advantage that a W/O emulsion spread on the skin dose not wash off readily with water.

All of the experimental formulas prepared and studied were not listed but only the two found to be the best of the long series. The emollient ingredients themselves had to be chosen carefully with not only their emollience in mind but lack of action as a primary irritant, potential allergenicity, compatibility and emulsifiability.

The surfactants to be employed were restricted to the nonionic type to avoid the irritating action of both anionic and cationic agents. A W/O emulsion which possessed all of the desirable features sought posed much greater technical problems than did an O/W product.

Since an emollient ointment is often used on cracked, tender skin, any preservative used might cause some irritation as the product penetrated these fissures. For this reason, no preservative was included in the W/O formula developed. It is conceivable, however, that the product, were it to be stored for long periods under unfavorable conditions, might require the addition of a suitable preservative to the aqueous phase. Such substances as the parabens or sorbic acid would be suitable for this purpose.

In evaluating the experimental formulas prepared, their physical appearance and stability were considered as well as their lubricity and smoothness when applied to the skin.

Another feature considered important was the ease with which the product could be rubbed "into the skin" leaving a somewhat occlusive emollient film but not one which was so greasy as to soil clothing appreciably. A great difference was found in the several products studied.

The following is considered to be the best water-in-oil emollient cream formulated.

Acetylated lanolin	90.0
Lanolins alcohol extract	120.0
Mineral oil	200.0
Microcrystalline wax	120.0
Sorbitan sesquioleate	20.0
Sorbitol solution	20.0
Purified water	430.0

Heat the acetylated lanolin, lanolin alcohols extract, liquid petrolatum, microcrystalline wax and sorbitan sesquioleate to 75° C. Add the other ingredients, previously warmed to the same temperature and stir until the mixture congeals and is completely cooled. Finally, homogenize at a temperature not exceeding 40° to improve texture and stability.

In this formula, certain ingredients are used which were selected for the following reasons. Acetylated lanolin has had most of the free hydroxyl groups of its constituent molecules esterified by acetylation.

The blocking of the hydroxyl groups makes the material much more hydrophobic. As a consequence, a film of acetylated lanolin on the skin is much more resistant to water. The product is also more emollient in its action on the skin and its allergenic properties are reduced. The lanolin alcohols extract used is a product that has been freed of alcohols having a destabilizing effect on emulsions. It not only has an unusual skin softening and emollient effect but its low interfacial tension toward water makes it of outstanding value as a stabilizer for water-in-oil emulsions.

The microcrystalline wax is a mixture of hydrocarbons which together with liquid petrolatum gives a product similar to white petrolatum but one which is far superior in that it rubs into the skin much better and does not leave the skin as greasy as does petrolatum. The sorbitol solution was included for the purpose of providing some water-soluble moisture retaining material.

The ointment is improved in both texture and stability by homogenization as a final step at a temperature not exceeding 40 degrees. Higher temperatures will cause the emulsion to break. The hand homogenizer gives excellent results and can be used as a finishing step on a small scale. This ointment has what are believed to be excellent qualities as an emollient. Clinical testing by two dermatologists has shown it to be a useful therapeutic agent in treating excessively dry skin and to have good patient acceptance.

The formula for this emollient ointment has been submitted through subcommittee #9 (external preparations) for consideration as an official preparation in the *United States Pharmacopeia.*

A suggested oil-in-water emulsion is the following:

Stearyl alcohol	130.0
White petrolatum	150.0
Acetylated lanolin	150.0
Lanolin alcohols extract	50.0
Sorbitan sesquioleate	20.0
Polyoxyl 40 stearate	50.0
Propylene glycol	120.0
Methyl paraben	0.25
Propyl paraben	0.15
Purified water	330.0

Heat the stearyl alcohol, white petrolatum, acetylated lanolin, lanolin alcohols extract, and sorbitan sesquioleate to 75°. Add the other ingredients in water previously warmed to the same temperature and stir until the mixture congeals.

This cream is very stable and possesses excellent cosmetic properties.

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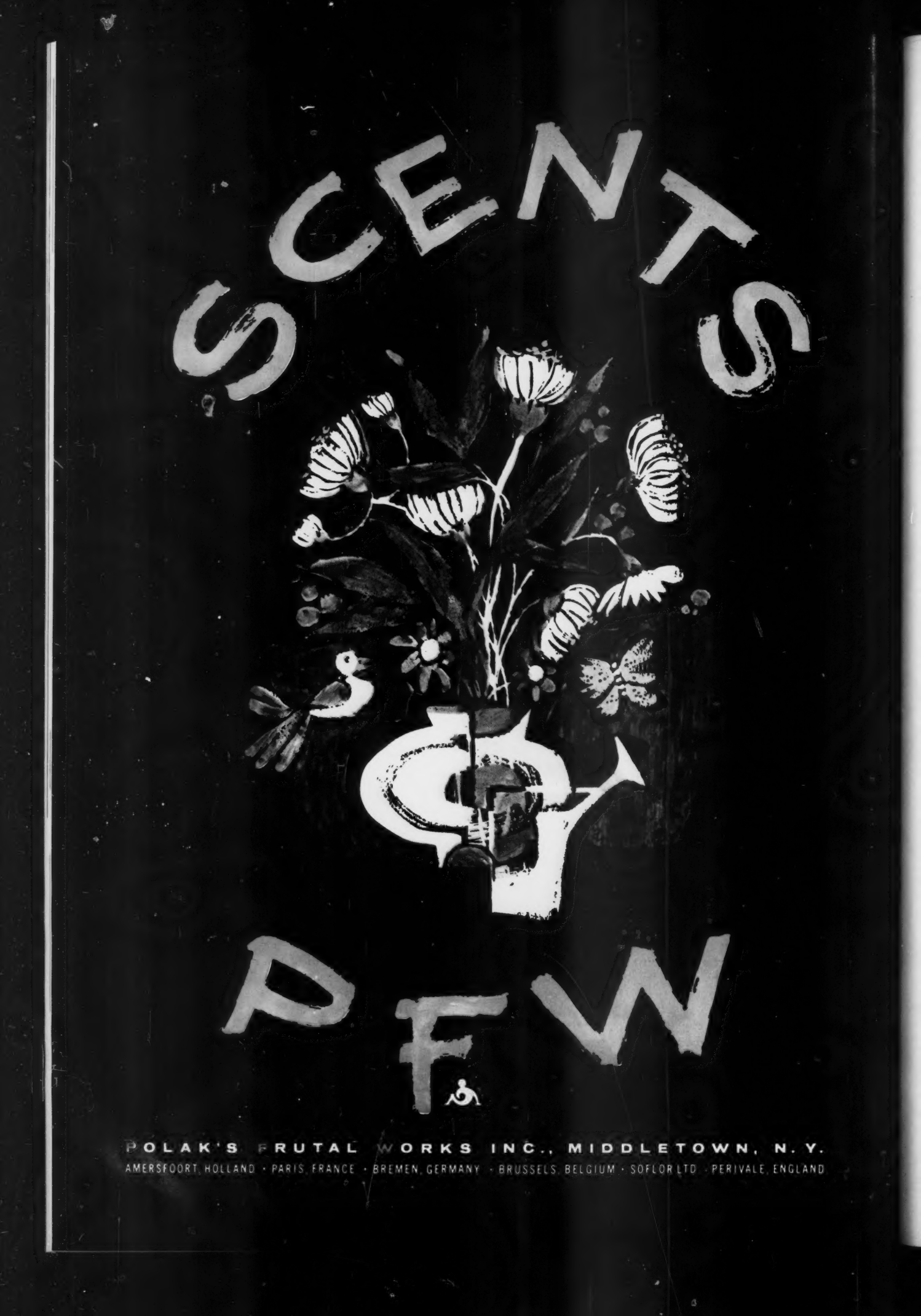

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Overcoming Bitterness

Several months ago I tried to follow up a report in *Chemical Abstracts* about a compound, potassium gymnemate, that interfered with the sweetness of saccharine, but got nowhere. Now, doing what should always be done first, I looked up the compound in *The Merck Index*, and it looks very interesting indeed, as a research tool or even as a flavor component for masking bitter medicinals. As our own T. R. Farrell said, "Anyone who read the whole *Merck Index* would know about it." Gymnemic acid, $C_{32}H_{55}O_{12}$, is an acid of glucosidal character occurring as the potassium salt in the leaves of *Gymnema sylvestre* and allied *Asclepiadaceae*. It completely obtunds taste for several hours for bitter or sweet, e.g., quinine or sugar, but not for sour, astringent or pungent substances. References: Hooper, *Chem. News* 59: 159, 1889; Mhaskar, *Ind. J. Med. Res.* No. 16, 1, 1930.

The compound certainly warrants considerable investigation, for toxicity determination, its mechanism of action, its structure and related synthetic compounds that might have a similar effect.

Ceylon Lemongrass Oil

Lemongrass from the *Gramineæ*, genus *Cymbopogon*, is a robust plant which grows as a tuft with numerous stiff stems at the base. There are two principal types of oil: West Indian obtained from *Cymbopogon citratus*, and East Indian obtained from *Cymbopogon flexuosus*. Oils from these two species differ considerably in physicochemical properties, especially in solubility in alcohol, West Indian lemongrass oil being less soluble in 70 per cent alcohol.

Cymbopogon citratus is known only in cultivation, although some authorities claim that it occurs in the wild state in Java. *Cymbopogon flexuosus* is cultivated on only a small scale in Ceylon and is a native of the southern part of India. The bulk of the island's supply according to M. G. De Silva (*Manuf. Chem.* 30: 415, 1959) is from *Cymbopogon citratus* which is cultivated in the extreme south of Ceylon and also on a small scale in Peradeniya.

Analysis of the citral content from the leaves of lemongrass of different ages, selected in order of formation, shows an increase in citral content from the first formed leaf up to the fifth leaf.

The citral content of oils obtained from thick tubers varies from 10 to 12 per cent. However, fibrous roots do not contain appreciable quantities of oil. In the tubers, as in the leaves, the oil content decreases with age.

The leaves are cut three or four times a year; each cutting gives 5,000 to 7,000 lb. per acre. The grass is distilled while fresh to avoid the loss of oil which occurs if it is left to dry.

The yield of lemongrass oil varies from 0.3-0.4 per cent, depending upon the season and the plant material.

The oil is bottled and kept for a few days to allow water and other deposits (usually copper salts) to separate, and it is then transferred to iron drums.

Lemongrass oil has an intense lemon-like odor and taste and is reddish-yellow to reddish-brown in color.

Citral is the most important constituent and is present as a mixture of at least two stereoisomers, α-citral and β-citral, varying from 70-85 per cent in normal oil.

The oil has a fairly high content of terpenes together with the citral and this latter can be concentrated by distillation in vacuum.

Citral, the main isolate of the oil, forms the basis of many synthetics. The most remarkable of these are the ionones, which are normally made by the condensation of citral with acetone and then heating with concentrated sulfuric acid to invert pseudoionone to ionone.

As lemongrass oil contains a mixture of both saturated and unsaturated compounds, the chemical nature of the oil changes on standing. This is probably due to the polymerization of the terpenes. Citral, the major constituent, has one aldehydic and two ethylenic linkages. Hence, it is readily attacked by oxidizing agents. On exposure to air citral oxidizes easily, so that the reddish-brown color changes, becoming more yellow.

Like most essential oils, lemongrass oil is adversely affected by air, heat and light and it must be stored carefully. In properly sealed containers it will keep in good condition for years. When exposed for a few weeks it changes considerably.

The quality of lemongrass oil is best determined by its citral content. In normal oil this varies from 65 to 68 per cent Two methods sodium bisulfite and sodium sulfite are used to determine citral content. The former method gives higher values (2-5 per cent), as it determines a part of methyl heptenone with citral.

With its intensive, fresh and persistent lemon-like odor lemongrass oil finds its main applications in perfumery. Lemongrass oil also contains 10-20 per cent of myrcene, which itself has wide perfumery applications. According to Pickthall, myrcene performs well in milled toilet soaps.

By distilling lemongrass with sodium bisulfite 100 per cent citral can be obtained. When used in soap 98-100 per cent citral gives a good lemony odor after one month, but after six months this fades. The soap is also liable to yellow slightly, although wrapped samples fade less.

Bath Perfumes

Perfume for bath preparations must be strong in odor and readily volatile in the warm water according to V. Vasic (*Manuf. Chem.* 30: 366, 1959). The fragrance of pine scents, such as pine needle oil, dwarf pine oil, silver fir oil, spruce needle oil, etc., is ideal for bath preparations. Eau-de-cologne and lavender, together with their heavier modifications and fougere type of perfumes, run close in popularity to the pine perfumes. Jasmin, gardenia, rose and lilac are also used and many bouquet odors give good results.

Heavy fancy compositions or sweet floral perfumes are unsuitable for bath preparations.

In developing the perfume for bath salts particular attention should be given to possible reaction between its ingredients and the basic salt mixture. The perfume-color combination must be of such a nature that it will not be reactive and therefore not cause changes in color or odor. This is not a problem involving conditions of use so much as of shelf storage, which is usually from six months to one year.

Many perfume compounds are unsuitable for making a perfume for bath crystals because they deteriorate quickly in contact with the alkaline crystals. In general, perfume compounds designed for use in soaps are satisfactory in bath salts, although these are frequently more strongly alkaline than most toilet soaps. Certain otherwise very stable and useful perfume compounds and essential oils are excluded. Often changes may not be apparent when the bath salt is freshly prepared, as the faulty reaction will only make its appearance upon storage, and even then may depend upon varying climatic conditions.

Conifer oils are especially important in the compounding of bath salt perfumes. Petitgrain oil, citrus oil, sage oil and verbena oil are useful modifiers, whilst bornyl acetate intensifies the natural odor of conifer oils and eucalyptus oil makes it appear fresher. The use of a substantial amount of resinoid fixatives, such as resinoids of olibanum, galbanum, and of elemi, are of great assistance in improving the lasting qualities of a bath salt perfume.

Among synthetic perfumery materials, those with a highly diffusive power should be chosen, because of the necessity to volatilize in moist air. Bornyl compounds, benzyl acetate, phenyl ethyl alcohol, aubepine and traces of fatty aldehydes and fatty alcohols are most useful for this purpose.

The recommended concentration of perfume ranges from 0.5 to 5 per cent; 0.5 to 1 per cent of perfume is the usual quantity used.

The perfuming of bath salts is simple. The crystals are placed in a ribbon powder mixer, and a solution of the perfume, alcohol and the desired color is added to the crystals with mixing. After the crystals are uniformly colored, they are placed on trays to allow the alcohol to evaporate, and are then ready to be packed.

Liquid bath perfuming preparations can be considered a part of perfumery rather than cosmetics, for the main purpose of the product is to make a pleasant odor. Liquid bath perfuming preparations are of two main types: bath oils—an oily type not miscible or emulsifiable with water, so that the perfume oils are kept on the surface of the water; and bath essences—preparations soluble or emulsifiable in water.

The perfume types recommended for bath salts are equally suitable for bath oils and bath essences. The amount of perfume is dependent upon the type of perfume, solubility of perfume in the base, solubilizing effect of the solubilizing agent and the price of finished product, so that the perfume content may be anything between 5 and 25 per cent.

Bath oils are prepared by dissolving perfume in castor oil, with the viscosity adjusted by means of alcohol and the addition of an oil-soluble color, if desired. Other oils can be used for this purpose, but they are more difficult to perfume and color. Some of the synthetic oily esters may be used for such preparations, *e.g.*, isopropyl myristate, isopropyl butyrate and others. They can be easily perfumed and colored. The amount of alcohol is controlled primarily by the viscosity adjustment.

Bath essences are perfumes dissolved in solubilizing agents. In addition to the perfume, they contain a detergent that will eliminate calcium salt deposits which, together with the fatty acids from soap, cause a ring around the tub. The composition of the essence should be compounded so that it disperses uniformly in the water without separation of free perfume.

Originally sulfonated oils were mixed with the perfume for this purpose, but modern bath essences are based on the synthetic nonfoaming detergents with a perfume-solubilizing agent to keep the product clear. They are sometimes diluted with water to reduce the cost.

For the production of such transparent pseudo-solutions the polyoxyalkylene sorbitan esters are used —notably the monolaurate and mono-oleate—and certain of the polyoxyethylene ethers, based on alkyl phenols or castor oil.

For most perfume compounds three to five parts of solubilizer will solubilize one part of perfume compound in water, although with certain compounds as much as eight to nine parts of the solubilizer may be necessary to obtain a clear solution. To increase the solubility, co-solvents such as diethylene glycol monoethyl ether, ethyl alcohol and isopropyl alcohol are recommended. The non-ionic solubilizing agents act as fixatives and often enhance and mellow the bouquet of the perfume compound.

The concentration of perfume in bath oils may be increased so that only a few drops of oil are needed to perfume the bath. Such concentrated bath oils may be packaged in soft gelatin capsules. The perfume chosen must not attack gelatine.

Many different synthetic detergents which foam when water pressure is applied, and also powdered and liquid soaps, have been used for the formulation of bubble baths. The bubble baths of desired properties may contain also non-detergent surface-active agents, emulsifiers and sequestering agents. Natural and synthetic water-soluble gums are sometimes used in bubble bath formulas to impart properties not possessed by some detergents. These otherwise good foaming detergents will not keep dispersed soil from redepositing. Sodium carboxymethylcellulose has this property, and some bubble bath formulations contain small amounts of it to keep soil particles in suspension and to increase the viscosity to give the desired body to the liquid bubble bath.

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(*Continued from page 755*)

hols in the 8 to 12 micron region with the characteristic differences serving to identify the four compounds by comparison of their spectra with the I.R. curves of the reference materials. Usually the I.R. spectra serve as empirical "fingerprints" in which the various peaks have not been assigned to specific features of the molecule. In general, functional groups can be readily identified, often quantitatively, but elucidation of fine structure in a molecule must usually be reserved for more refined techniques. In the present case, the secondary absorption caused by the hydroxyl function is visible for all the alcohols and the shift from 9.5 microns in citronellol and dimethyl octanol to 10.0 microns in geraniol and nerol is explained by the alpha-beta unsaturation in the latter two cases. The more subtle effects of the cis-trans nerol-geraniol isomerism, although readily apparent, have not been explained by assignments. An experienced spectroscopist would know at this point that the four compounds were primary alcohols, two of them with alpha-beta unsaturation. This, combined with carbon-hydrogen analysis, molecular weight determination, boiling point, and physical constants, establishes them as C_{10} alcohols with no, one, or two double bonds.

The mass spectrophotometer separates ions according to their masses and establishes the molecular weights and relative proportions of the various components of a mixture. It replaces the older techniques of molecular weight determination with a rapid procedure of great precision. By splitting a certain percentage of the molecules into fragments which are again separated according to mass number, a characteristic mass spectrum is obtained which is another "fingerprint" of the particular compound and serves to identify it not only by comparison with reference spectra, but often by merely studying the masses and amounts of the various fragments formed and from this reconstructing the parent molecule on a theroretical basis. However, this is usually restricted to simple molecules.

Since the mass spectrograph separates ions according to their masses (strictly speaking, the mass must be divided by the charge) it is possible to obtain the mass spectrum by scanning the entire range and recording it either photographically or on a chart. Such a procedure takes a matter of minutes; an extremely small sample is sufficient and can be obtained by trapping a component from a VPC column as a gas, and feeding it to the mass spectrometer. The inert carrier gas helium, for example, can be removed by first cooling the entire sample in liquid nitrogen and pumping off most of the helium which gives a more concentrated spectrum.

Within the last three years, a new type of mass spectrometer called the Time-of-Flight has become available. It separates the ions of different mass on a time rather than spatial basis. This instrument gives the entire mass spectrum substantially instantaneously (as many as ten thousand spectra per second). It has thus been used successfully for monitoring the effluent from a VPC column directly, without the need for trapping.[2] The various components are identified by their mass spectra as they are eluted. It is possible also to study the composition of materials coming out as one peak, for if the mass spectrum remains substantially unchanged during the entire elution period of the peak, it is likely that only one component is present and that the peak represents homogeneous material. If, however, the mass spectrum changes during the life of the peak, it is proof that the peak represents an incompletely resolved mixture.

The newest spectral technique, and also the most complicated, most expensive, and most sophisticated, is that of nuclear magnetic resonance. Atoms with nuclear magnetic moments give such spectra. Thus hydrogen is visible by these techniques—carbon and oxygen are not. However, the ubiquitous hydrogen atom shows up at various positions in the NMR spectrum depending upon the nature of the chemical group of which it is a part and its relationship to other groups. An analysis of these spectra can elucidate the structure of molecules as complicated as the C_{10} terpene alcohols. A detailed discussion of this technique is beyond the scope of the present paper but the NMR spectra of geraniol and citronellol (Fig. 4) will show, in general, the principles involved. The geraniol spectrum reveals five major peaks, or groups of peaks, corresponding to five different kinds of chemically bound hydrogens. Both rigid theoretical treatment and practical experience, based upon known reference materials with similar groupings, can be used to identify these hydrogens. The areas under the peaks are directly proportional to the number of hydrogens causing the perturbation. The amount of splitting is in general a function of the number of hydrogens on the adjacent carbon. Using these principles leads to the following summary: Peak (c) consists of two incompletely resolved triplets due to hydrogens on olefinic carbon alpha to CH_2 ($=CH-CH_2-$). Peak (b), a doublet, reveals by its position that it is caused by the hydrogens on a carbon containing a hydroxyl. The area corresponds to two such hydrogens, thus the compound is a primary alcohol. The doublet nature and shift of the peak position are caused by one hydrogen on the alpha carbon atom and an unsaturated alpha carbon atom. The position and sharpness of the hydroxyl hydrogen peak (a) are confirmation of the alpha-beta unsaturation in the molecule, which prevents hydrogen bonding which would broaden or blur the peak. Peak (d) is due to hydrogens alpha to a double bond; there are two pairs of such hydrogens, one alpha to a carbon with no hydrogens and one alpha to a carbon with one hydrogen, so that half of

(*Continued on page 830*)

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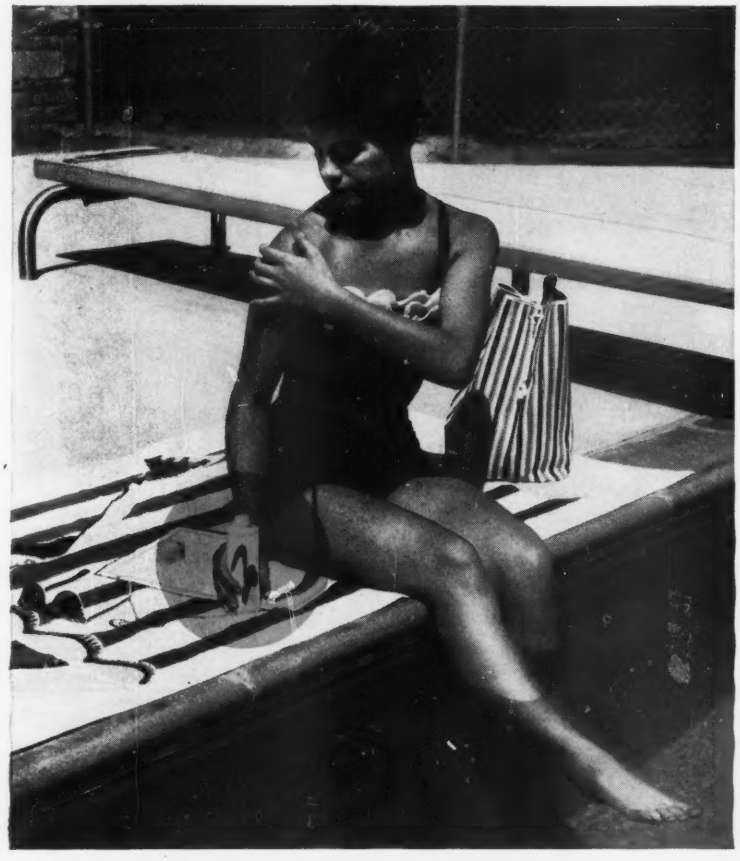

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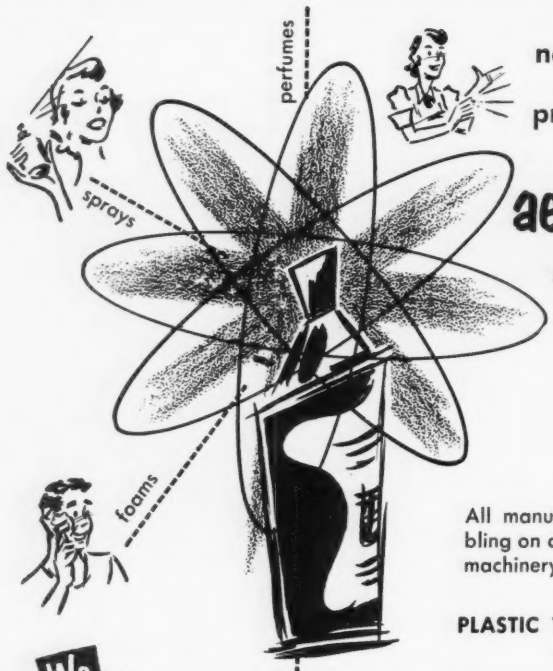

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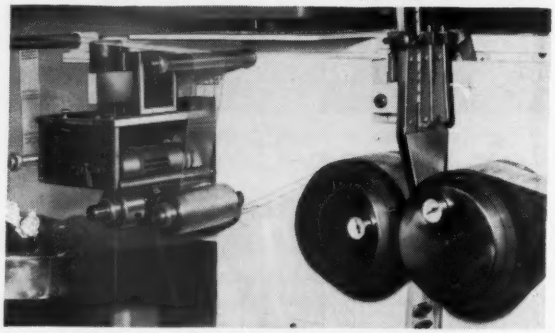

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Skin Research

Tissue Reactions

Several experiments making use of albino rabbits as test animals have been performed by J. T. Prior and G. A. Cronk (*A.M.A. Arch. Dermatol.* 80:447, 1959) to study the tissue reactions to subcutaneous and intracutaneous injections and to percutaneous application of a variety of aluminum salts and zirconium tetraisopropoxide.

Acute inflammatory reactions with tissue necrosis and ulceration were noted in association with the subcutaneous and intracutaneous injection of the aluminum compounds. There was a more marked reaction at the injection sites in areas that had been previously injured. Repeated injections, either subcutaneous or intracutaneously, resulted in the same type of cutaneous ulcers, but these were not felt to be more severe than those following the original injections. Granulomas were seen only after the subcutaneous injection of aluminum chlorohydroxide complex. All lesions went on to normal, although delayed, healing. The percutaneous application of these chemical compounds failed to produce any significant lesions.

The zirconium compound produced significant subcutaneous and intracutaneous recations only when combined with hexachlorophene. Ulcerative lesions were produced only in areas in which there had been previous injury. Percutaneous application of the zirconium-hexachlorophene mixture produced no changes.

Chloroquine Hair Depigmentation

Ten cases of decrease in reddish or blonde hair color following chloroquine diphosphate are reported by T. S. Saunders et al (*J. Invest. Dermatol.* 33:87, 1959). Its absence in black-haired individuals was noted. The decrease was reversible in every case following withdrawal of the drug. Chloroquine, when fed to flies and guinea pigs failed to produce any color change. However, feathers of the Rhode Island Red chick were depigmented by instillation of chloroquine into the yolk sac. Under the same conditions, there was no change in pigmentation in the Black Minorca chick.

These observations and experiments indicate that chloroquine interferes with the pigment formation in blonde-red haired humans and in chicks of comparable coloring. The nature of the metabolic block awaits further investigation.

Zirconium Granulomas

In the February 1958 issue of this magazine, page 231, we commented "It may be wise for tests to be made with dilute suspensions of zirconium carbonates and hydroxides to determine their ability, if any, to generate an allergic hypersensitivity response." We were assured, before and after the printing of this suggestion, that in literally millions of cases in which insoluble zirconium compounds had been used in treating poison ivy, no instances of zirconium granulomas had been encountered, that hypersensitivity responses occurred only with the soluble zirconium salts incorporated in deodorant sticks. Now R. M. Williams and G. B. Skipworth report in the "A.M.A. Archives of Dermatology" volume 80, p. 273, 1959 two instances of granulomas from hydrous zirconium oxide. In the first case, the patient had repeatedly used a zirconium lotion for the treatment of Rhus dermatitis, but a papular eruption remained on her arms and neck. She had never used a stick type deodorant. The eruption was shown to be granulomatous and vaccination on the thigh with the zirconium lotion resulted in the development of the same granulomatous reaction.

Another patient developed an underarm rash two months after using a commercial zirconium deodorant stick and subsequently developed a granuloma on her thigh after vaccination with a hydrous zirconium hydroxide suspension. The authors concluded that these cases indicated allergic sensitization to the zirconium ion rather than to a specific salt of zirconium or impurity.

Vitiligo Treatment

Data from cytological studies of 18 cases of vitiligo were presented by F. Hu et al. (*J. Invest. Dermatol.* 33:267, 1959). Included are 15 cases of typical vitiligo, 2 cases of congenital vitiligo and 1 case classified as pseudovitiligo.

Results appear to indicate that a favorable response to combined methoxsalen and ultra-violet light therapy depends on 3 basic mechanisms: 1) the presence of melanocytes which are capable of forming pigment (shown by dopa reaction), 2) the capacity for proliferation and/or migration of active melanocytes from adjacent pigmented areas to vitiliginous areas, and 3) the ability of epithelial cells to receive pigment from the active melanocytes (shown by silver technic).

A factor, equal in importance to the presence of melanocytes capable of forming melanin pigment, seems to be operative in cases of vitiligo which fail to repigment following methoxsalen therapy. This factor is closely related to the transfer of pigment from the melanocytes to the epithelial cells. The best method for demonstrating this ability of pigment transfer is by silver staining.

COMING EVENTS . . . . .

1960

JANUARY

6 **Society of Cosmetic Chemists,** New York Chapter, monthly meeting, Hotel New Yorker, N. Y. C. (Dr. Saul Bell, S.C.C., 2 East 63rd St., N. Y. C.)

7 **Foragers of America,** annual banquet, The Stork Club, N. Y. C. (Wm. Hendey, Foragers Club Room, Midston House, 22 East 38th St., N. Y. C.)

9 **Northwest Society for Clinical Research,** Seattle, Washington (Dr. John R. Hogness, 721 Minor Ave., Seattle 4, Wash.)

11-13 **American Academy of Allergy,** Hollywood Beach Hotel, Hollywood Fla. (James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wisc.)

21-22 **Folding Paper Box Assn. of America,** National Folding Carton Production Forum, Statler Hilton, N. Y. C.

FEBRUARY

2-4 **Society of the Plastics Industry,** Reinforced Plastics Division conference, Edgewater Beach Hotel, Chicago, Ill. (S.P.I., 250 Park Ave., N. Y. C. 17)

3 **Society of Cosmetic Chemists,** New York Chapter, monthly meeting, Hotel New Yorker, N. Y. C. (See above.)

3-5 **Pharmaceutical Manufacturers Assn.,** Legislative Section, Boca Raton, Fla. (Dr. Karl Bambach, P.M.A., 1411 K Street, N.W., Washington 5, D.C.)

8-10 **Pharmaceutical Manufacturers Assn.,** central regional meeting, Edgewater Beach Hotel, Chicago, Ill. (Dr. J. O'Neill Closs, 1411 K Street, N.W., Washington 5, D.C.)

15-16 **Pharmaceutical Manufacturers Assn.,** western regional meeting, Ambassador Hotel, Los Angeles, Calif. (Dr. J. O'Neill Closs—see above.)

25-27 **Symposium on Fundamental Cancer Research,** Univ. of Texas, Houston, Texas (Univ. of Texas, M.D. Anderson Hospital and Tumor Institute, Houston 5, Texas)

28 **American College of Allergists** (through March 5) Americana Hotel, Bal Harbour, Miami Beach, Fla. (Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Minn.)

MARCH

2 **Society of Cosmetic Chemists,** New York Chapter, monthly meeting, Hotel New Yorker, N. Y. C. (Dr. Saul Bell, S.C.C., 2 E. 63rd St., N. Y. C.)

2-4 **Pharmaceutical Manufacturers Assn.,** Medical Section, Hollywood Beach Hotel, Hollywood Fla. (Dr. Karl Bambach—see above.)

3 **Drug, Chemical and Allied Trades Association, New York Board of Trade, Inc.,** annual dinner (Helen L. Booth, D.C.A.T., One Liberty St., N. Y. C. 5)

13-18 **National Health Council,** national health forum, Miami, Fla. (Philip E. Ryan, 1790 Broadway, N.Y.C. 19)

15-16 **American Broncho-Esaphogological Assn.,** Deauville Hotel, Miami Beach, Fla. (Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Penna.)

15-17 **American Laryngological, Rhinological and Otological Society,** Deauville Hotel, Miami Beach, Fla. (Dr. C. Stewart Nash, 708 Medical Arts Building, Rochester 7, N.Y.)

18-19 **American Laryngological Assn.,** Deauville Hotel, Miami Beach, Fla. (Dr. Lyman Richards, Massachusetts Institute of Technology, Cambridge 39, Mass.)

22-23 **Pharmaceutical Manufacturers Assn.,** Pharmaceutical Contact Section, Shoreham Hotel, Washington, D. C. (Dr. Carl Bambach, P. M. A., see above.)

APRIL

1-2 **American Gastroenteral Assn.,** Roosevelt Hotel, New Orleans, La. (Dr. Wade Volwiler, Dept. of Medicine, University of Washington, Seattle, Wash.)

1-3 **American Society of Internal Medicine,** Mark Hopkins Hotel, San Francisco, Calif. (Robert L. Richards, 350 Post St., San Francisco 8, Calif.)

2-6 **American College of Obstetricians and Gynecologists,** Netherland Hilton Hotel, Cincinnati, Ohio (Donald F. Richardson, P. O. Box 749, Chicago 90, Ill.)

4-7 **American Management Assn.,** national packaging exposition, Convention Hall, Atlantic City, N.J. (Packaging Exposition, Clapp & Poliak, Inc., 341 Madison Ave., N.Y.C. 17)

5-14 **American Chemical Society,** spring national meeting, Cleveland, Ohio (A. T. Winstead, A.C.S., National Meetings Dept., 1155 Sixteenth St., N.W., Washington 6, D. C.)

8-12 **American Dermatological Assn.,** Boca Raton Hotel, Boca Raton, Fla. (Dr. Wiley M. Sams, 308 Ingraham Bldg., Miami 32, Fla.)

11-15 **American Assn. of Immunologists,** Chicago, Ill. (Dr. Calderon Howe, Columbia University College of Physicians and Surgeons, N.Y.C. 22)

11-16 **American Society of Biological Chemists,** Chicago, Ill. (Dr. Frank W. Putnam, Dept. of Biochemistry, Univ. of Fla., Gainesville, Fla.)

20 **Society of Cosmetic Chemists,** New York Chapter, monthly meeting—ladies' night, Hotel New Yorker, N. Y. C. (Dr. Saul Bell, S.C.C., 2 East 63rd St., N. Y. C.)

28-30 **American Assn. of Pathologists and Bacteriologists,** Hotel Peabody, Memphis, Tenn. (Dr. Russell L. Holman, Dept. of Pathology, L.S.U. School of Medicine, New Orleans, La.)

MAY

8-11 **Proprietary Association,** annual meeting, The Greenbrier, White Sulphur Springs, W. Va. (Dr. Howard A. Prentice, 810 18th St., N.W., Washington 6, D.C.

11 **Toilet Goods Assn.,** Scientific Section, Waldorf-Astoria Hotel, N.Y.C. (Kathryn Fitzpatrick, Americas Bldg., Rockefeller Center, N.Y.C. 20)

11-13 **Synthetic Organic Chemical Manufacturers Assn.,** annual spring outing, Shawnee-on-Delaware, Penna. (S. Stewart Graff, S.O.C.M.A., 41 East 41st St., N. Y. C. 17)

16-18 **Chemical Specialties Manufacturers Assn.,** mid-year meeting, Drake Hotel, Chicago, Ill. (C.S.M.A., 50 E. 41st St., N.Y.C 17)

JUNE

12-15 **Extension Services in Pharmacy,** annual national industrial pharmaceutical research conference (stabilization and stability testing of pharmaceuticals), King's Gateway. Land O' Lakes, Wisc. (Richard S. Strommen, E.S.P., Univ. of Wisconsin, Madison, Wisc.)

27-30 **Toilet Goods Assn.,** annual convention, Poland Spring, Maine, (Kathryn Fitzpatrick, Americas Bldg., Rockefeller Center, N.Y.C. 20)

JULY

19-21 **Western Packaging & Materials Handling Exposition,** Pan Pacific Auditorium, Los Angeles, Calif. (Western Packaging Exposition, Clapp & Poliak, Inc., 341 Madison Ave., N. Y. C. 17) ●

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(Continued from page 824)

the double peak has a contribution from both groups and is stronger than the other. Peak (e) is due to methyl hydrogens alpha to doubly bonded carbon, the area of the peak corresponding to three methyls. The absence of any further peaks reveals a very significant fact, that every hydrogen in the molecule is either on or adjacent to an olefinic carbon.

A simple, logical correlation of these data lead to the already known structure for geraniol as the only interpretation consistent with all the facts. A more rigid analysis could show differences even between geraniol and its cis isomer Nerol.

The NMR spectrum of citronellol can be analyzed in a similar manner. Here it need be pointed out only that there is but one triplet (c) corresponding to olefinic hydrogen; the peak for the hydrogens on the hydroxyl carbon is now a triplet (b), since the adjacent carbon has two hydrogens which cause splitting; the hydroxyl hydrogen (a) is less sharp because of its ability to hydrogen bond; and there are further peaks (f) and (g) to the right of the spectrum corresponding to methylene and methyl hydrogens not adjacent to olefinic carbon atoms. All these features, both qualitative and quantitative, check precisely with the known structure of citronellol.

The above discussion has concerned itself with an *a posteriori* proof of structure of already known compounds. The use of these techniques for establishing theoretically predicted, but unproved, structures is shown in the proof of the structure of the isomers of alloocimenol formed by the hydrochlorination and subsequent hydrolysis of alloocimene.[3]

The pyrolysis of α-pinene to alloocimene, the subject of a number of careful studies[4-9] is greatly facilitated by evaluation of the pyrolyzate with VPC techniques. Here the large number of products formed require, for complete resolution, the aforementioned superior performance of a capillary instrument. Figs. 5 and 6 show the relative performance of a well-functioning conventional packed column versus a capillary column using a beta ionization gage detector for greater sensitivity. Ultraviolet spectral analysis, of no use in the previous example which dealt with materials without ultraviolet chromophores, is most effective to determine the alloocimene content of the pyrolyzate. The magnitude of the ultraviolet absorption at 270 to 280 millimicrons, characteristic of a triply conjugated system, is therefore specific for the two isomers of alloocimene. These two isomers have their λmax. about five millimicrons apart, so that a mixture is not resolved on UV, the peak falling somewhere between that of the two pure isomers. Again, by VPC these isomers are readily separated.

After hydrochlorination and hydrolysis, three isomeric alcohols can be expected on a theoretical basis. Again, fractional distillation failed to separate these close boiling isomers but VPC showed the three as

components of the product. Trapping successfully separated these isomers, which were identified by their infrared spectra. As a final proof of structure the three isomers were prepared synthetically and the I.R. spectra of these synthetic materials checked exactly with the three components trapped from the above mixture.

In summary, this paper discusses the application of the various spectroanalytical techniques—ultraviolet, infrared, mass, nuclear magnetic resonance, and the separation technique of vapor phase chromatography—to the structure-proof of a number of fragrance materials. A mixture of primary terpene alcohols of known composition is separated and analyzed and the structures of geraniol and citronellol are derived using these techniques alone. Mass spectra of the terpene alcohols, as obtained with the newly developed Time-of-Flight mass spectrometer, are compared with those from a space magnetic type instrument. Special emphasis is given to a discussion of the data available from a careful analysis of nuclear magnetic resonance spectra of the same terpene alcohols.

The synthesis from α-pinene of a new fragrance material "alloocimenol," which is a mixture of several isomeric alcohols, is presented together with the use of the above instrumental methods in facilitating the development of the process. A comparison is shown of the resolution of a complex mixture of terpenes using a packed VPC column, and the newly developed capillary column.

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ANOTHER KISSING DISEASE

(*Continued from page 757*)

One primary or small herpetic circumscribed lesion usually spreads and coalesces to embrace an ever widening area. Protective factors seem to be necessary, therefore, for effective local therapy; furthermore, the local burning, itching, and tingling symptoms also call for medicinal relief. A new preparation embracing these objectives has appeared recently. It incorporates resorcinol 2 per cent, sulfur 8 per cent, hexachlorophene 0.25 per cent, and alcohol 11

(*Continued on page 834*)

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Trade Literature

Syntex

Syntex S.A., Apartado 2679, Mexico City, Mexico, has issued a 60-page bulletin in color and illustrated, which describes the Syntex operation, its program of research, the executives of the organization, and contains a statement concerning the importance of steroid hormones, one on new possibilities for steroids, and a listing of Syntex products with specifications for its sex hormones, cortical hormones, anabolic agents, and intermediates.

Engraving on Metal

The Lambert Engraving Company, Inc., Attleboro, Mass., has published a four-page booklet in full color describing with illustrations the finishes and sculptured effects achieved by cutting into metal by the company's exclusive "multitool" process, which produces hand-engraved appearance at modest cost, in an unlimited number of designs ranging from delicate florals to massive moires.

Annual Nielsen Review

The 25th Annual Nielsen Review of retail drug and proprietary store trends has been released by the A. C. Nielsen Company, 2101 Howard St., Chicago 45, Illinois. The 28-page report is divided into five sections: sales trends of drug and proprietary stores, comparative trends of drug and grocery stores, other characteristics and trends, impact of national economy, and observations and comments. Charts and tables throughout the publication amply illustrate the text itself.

The Salesmen's Boner

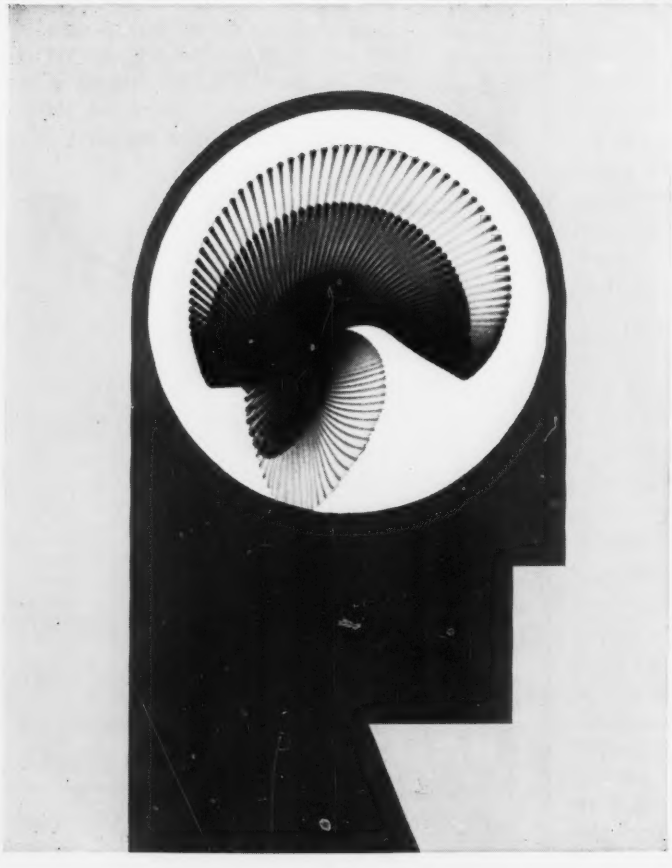
The costliest boner made by today's salesmen is not selling from the customer's viewpoint, according to more than 800 sales chiefs interviewed by Ted Pollock, whose six self-training pocket manuals are now available at 50 cents each and in quantity prices from the Sales Training Division, Pamphlet Press, P. O. Box 732, Brooklyn, New York.

Tuberculosis Control

The National Tuberculosis Association has released its 1959 Annual Report. The 32-page illustrated bulletin describes the three-point attack on TB: detection, treatment, and research. The work of the Association during the past year is presented in detail, along with the treasurer's report. A list of officers and directors of the Association, and those of the American Trudeau Society, its medical section, is appended, as well as the names of those with grants-in-aid, the institutions where they are working, and the subject of study. NTA resident and research fellowships are also included, along with names and addresses of constituent associations of the NTA.

Organon Brochure

Organon Inc., Orange, New Jersey, has published a brochure, Organon throughout the World, to mark the opening of its new laboratories, offices, and processing facilities in West Orange, N. J. It is designed to acquaint members of the trade and the medical profession with the organization.



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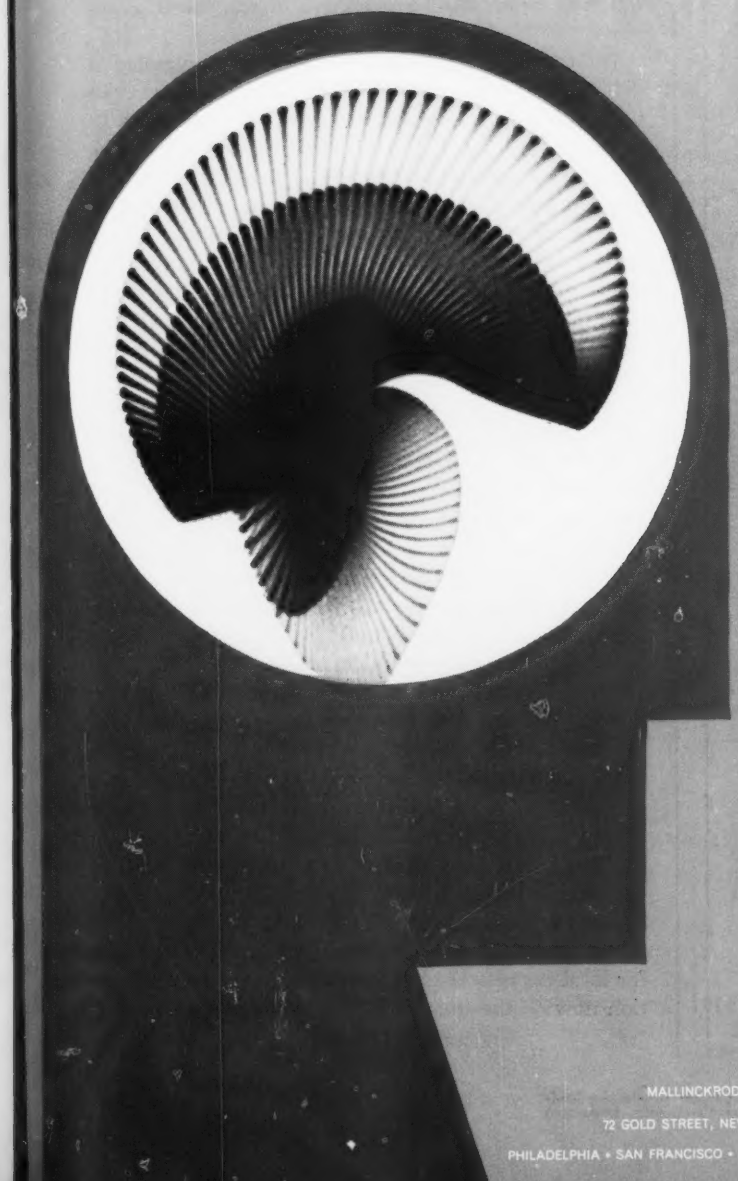

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AMERCHOL PARK . . . EDISON, N. J.

(*Continued from page 831*)

per cent, in a stable grease-free base. Such a base might include talc, bentonite, or chalk combined to form a heavy, dehydrating and long-lasting contact and protective coating over labial membrane lesions. This prolonged contact of the incorporated antiviral agents appears to be essential to successful prophylactic and therapeutic management of local herpes lesions. Since predisposing factors such as colds, influenza, and viral or bacillary pneumonias are treated by the physician as separate entities usually with general chemical or biological therapeutic agents, such generalized treatments have relatively little or no effect on the subsequent local herpes lesions.

Three significant observations deserve reporting.

(1) In non-medical cases, life guards with a history of frequent and prolonged herpes lesions on face and lips following long exposure to the sun used zinc oxide ointment as standard prophylaxis. However, over a long period of use, its effectiveness was obscure and, once the lesions developed, they progressed to full pathology of vesicular eruptions, swelling, and local pain, irrespective of the therapy applied.

On the contrary, when the druggist suggested a dehydrating base hexachlorophene preparation be used, the herpes lesions cleared up almost magically within a few days. Furthermore, if applied to the lips during the initial prodromal stages, the further development of watery blobs or secondary infection, apthous ulcers, and painful fissures or cracks which ordinarily heal so slowly was usually prevented. While sunburn lotions containing an ultra-violet filter might serve to prevent these eruptions, nevertheless, the hexylresorcinol, alcohol, sulfur, resorcinol in a dehydrating base as a prescription appears to be the best prophylactic agent yet devised.

(2) With predisposing factors resulting from prolonged exposure to extreme cold, with temperatures below freezing, several men in a labor gang habitually contracted herpes febrilis lesions, following colds and influenza. The local herpes lesions responded promptly to thinly spread topical applications of the R.S.H.A. inunction or T.I.D. Also, mild primary lesions failed to develop into the usually severe fulminating forms of simplex infections.

(3) Individuals suffering from herpes febrilis evidently resulting from febrile diseases or thermal and mechanical trauma, with subsequent dehydration that caused painful cracks and slowly healing fissures in the lips, responded suprisingly well to the new therapy.

From these observations two conclusions can be drawn. First, while further clinical data is obviously indicated, these preliminary case investigations suggest the possibility of a reasonable specific therapy for local herpes simplex lesions. Second, the preparation now on the market for the management of acne

(*Continued on page 836*)

Reader's Questions . . .

Skin Irritation: *I am engaged in the development of a number of new cosmetic products in which the active ingredients are synthetic organic chemicals that are not usually used on the skin. Can I guess in advance whether or not these chemicals will irritate or otherwise adversely affect the skin?* NEW YORK

I certainly would not assume from the structure of any compound not previously used on the skin that it is likely to be harmless; nor, as a corollary, would I assume from the structure alone that the compound is necessarily harmful. The presence of an amino or nitro group, or a fancy ring structure in the molecule may have little or no relationship to either safety or toxicity. As soon as possible in the investigation, when the potential usefulness of the new compound seems to warrant the expense of testing, safety determination should be undertaken. This involves tests on animals and then, after a large degree of safety has been proved, tests on an experimental group of human beings. Only after these safety assurances have been obtained may the test marketing of the product start. Requirements for a new drug application, where the new chemical can be expected to alter the skin and thus have a drug effect, are even more stringent.

Minimum animal tests must include the possibility of primary irritation on the skin and, if the preparation is used near the eyes, tests of eye irritation. When these tests are satisfactorily surmounted, patch tests on human subjects are advisable. This is often followed by sensitivity testing to determine possible allergenicity. At this relatively early stage of testing, percutaneous absorption may not be a factor, but the possibility should not be far removed from the mind of the investigator. This absorption may be desirable in certain pharmaceuticals, but systemic activity following absorption through the skin is not usually acceptable in cosmetics. Somewhere along the line there must be some knowledge of internal toxicity in case of accidental ingestion. Safety testing is expensive, but essential.

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AMERCHOL PARK . . . EDISON, N. J.

(*Continued from page 834*)

vulgaris, namely, Acnomel, contains resorcinol 2 per cent, sulfur 8 per cent, alcohol 11 per cent, and hexachlorophene 0.25 per cent in a stable, grease-free base.

SCHERING'S QUALITY CONTROL

(*Continued from page 764*)

expensive or poisonous drugs; proper storage and rotation of shipping room, label room, and warehouse stocks to prevent deterioration, damage, or accidental substitution. A dead stock area is also maintained to keep defective materials away from the movement of perfect goods.

Operating under the assumption that a well-informed worker can contribute much to the quality of a product, standard operating procedures are always available to any worker who must use them. These are written instructions for any operation explaining what to do, how to do it, when to do it, the sequence to be followed, what equipment to use, and all precautions to be observed.

Identification, a cardinal principle in the drug industry, is one of the best safeguards in preventing mix-ups and accidental contamination. Identification is accomplished by proper labeling of the finished products and the incorporation of a registered control number.

The control number appearing on Schering's sales packages contains the life history of that particular product. From the control number on the individual package can be determined the raw materials for the product and their origin, a description of all manufacturing processes, an identification of machines, people, tests, and analyses run on the product, and other pertinent data.

Documentation is an organized means of collecting in written form a complete history of every batch produced. Materials accounting is a system of checks and double checks to reveal deviations from prescribed limits. Inspection is an organized system of examinations to confirm good workmanship and uniformity at all points in the life of a product. Statistical inspection techniques are often employed.

Sanitation control prevents contamination from any source through a controlled program of cleanliness. Another important area of quality control is auditing control. Its responsibilities include: collection of samples; chemical analyses for assay, purity, identity, and physical properties; testing for special characteristics; packaging materials certification; filing control documents; filing of product samples; evaluation of returned goods; stability studies on finished products; periodic stock surveys; and surveys requiring special techniques related to safety, product contamination, or sanitation.

Employee selection and training can be considered

a valid function of quality control. In the final analysis, quality control is the employees who, with their special skills, experience, attitudes, morale, habits, and judgments, must spell success or failure to any quality control program.

As an example of the extensive effort Schering puts behind the quality control of a single product, Coricidin is a typical oral preparation. This is a red, coated tablet containing 2 mg. of chlorpheniramine maleate, 230 mg. of acetylsalicylic acid, 160 mg. of phenacetin, and 30 mg. of caffeine. A typical lot will contain 1.8 million tablets, with a time lapse of 28 days from raw materials to finished package; the time required for quality control tests is 12 days. The 4 active ingredients require a total of 38 tests; the Coricidin core, before coating, must undergo 14 tests including the measurement of disintegration time; the finished coated tablet is submitted to 16 additional tests for a grand total of 68 tests. Others, which can not be specifically enumerated, add to the total. Excipients, bulking agents, binders, disintegrators, lubricants, must all be tested and passed before they can be used in making the tablet. The entering raw material is sampled in the inspection area and then kept in the detention area until the laboratory approves the shipment. Coricidin cores and finished tablets are also held out of the process until they have been approved. Glass undergoes polariscope examination; bottles, caps, printed labels, boxes, etc., are selected for examination by random sampling. At 15-minute intervals during the tablet compressing operation which makes the cores, samples are taken and checked for size, weight, disintegration, and physical characteristics. Coating is a multi-step operation involving batches of 144,000 tablets; after each coat, samples are checked for weight, thickness, diameter, and uniformity. In the packaging stage, frequent counts are made to assure the proper number of tablets in each bottle and the correct number of bottles in the carton. A sample of each batch is tested in mice for freedom from toxicity, another sample is placed in stability storage to check shelf life, and a file sample is kept for possible future reference. Little enough is left to chance.

CLOSURES TODAY AND TOMORROW

(Continued from page 769)

improved by proper scientific thread design, improvements in molding powder formulations, and better control of molding techniques.

Originally, flat-bed, hand-operated presses were used with the closures manually unscrewed. Today, automatically operated, high-speed, electronically controlled equipment is in general use. Today's caps are more nearly uniform, for the human factor has been largely eliminated by automatically operated

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machines.

Closures molded from the phenol-formaldehyde resin have very good chemical resistance but, due to the wood flour filler, they are somewhat sensitive to dimentional change when stored in humid atmospheres, tending to increase in diameter under these conditions, although they resume their original dimentions upon drying. If the slight increase in dimensions tends to cause loosening of the caps when the capped bottles are exposed to higher humidities than those at the time of capping, it has been found practical to prehumidify the closures, thus increasing their dimensions before capping, and then cap with proper torque force. Should the pre-conditioned closures applied on the containers dry completely prior to removal, they will require a higher removal force, of course, but this expedient eliminates loose caps.

Urea-formaldehyde closures are somewhat more susceptible to the action of humidity and moisture than the phenol-formaldehyde type, and should not be used with steam sterilization. Melamine resins of higher cost, which can be produced in the pastel shades, will resist both steam sterilization and repeated wetting with water.

The thermosetting molded caps, as has been said, are somewhat affected by moisture and humidity. Many products contain water which, of course, would be picked up by the closure were it not for the liner in the cap, which is chosen not only for its resistance to the product but also for its moisture permeability. With the proper liner, the moisture from the product will not come in contact with the closure.

The susceptibility of the thermosetting molding materials to moisture makes ring gaskets of rubber or flowed-in compounds impractical, even though they may be thought superior as container seals for caps. When exposed to aqueous creams, gasket-lined jar covers have been found to crack in the top portion after several weeks of exposure at room temperature.

Thermoplastic Closures

Only thermosetting materials were available for many years, but, after the development of polystyrene molding compounds in 1938, closures could be injection-molded. Polystyrene compounds could be produced in transparent colors by means of dyes, or in opaque colors by means of pigmented fillers. Polystyrene has excellent resistance to the inorganic acids and alkalies, which made possible closures for the strong mineral acids to replace the costly ground-glass stoppers formerly used. The use of polystyrene for closures was not generally accepted in the industry; the price was too high. However, as the molding material was reduced in cost and injection-molding machines were improved, its use took on greater possibilities.

In the last two or three years, modification of polystyrene has been accomplished, producing three

types: the regular polystyrene, which is inclined to be glass-like or brittle, and two other grades—medium-impact and high-impact molding compounds. The latter two produce closures more resistant to tight application forces in high-speed machines.

Many thermoplastic molding compounds produce caps that are strong and resist dimensional change even when exposed to high humidity or moisture. High-impact polystyrene lends itself admirably for the production of liquor closures, especially for products that might be shipped by water, when temperature and humidity could be high.

Under similar conditions, the thermosetting closures may increase in demensions and become loose on glass containers. High-impact polystyrene with its excellent moisture resistance is suggested for molded closures for sealing pharmaceutical products shipped by water or exported to the tropics. It produces a more attractive closure that will not rust or deteriorate under such climatic conditions.

Following polystyrene, low-density polyethylene became available. This does not lend itself to use in screw caps; it is too flexible and distorts when the cap is screwed into place—the threads tend to jump. On the other hand, low-density polyethylene can be used in snap caps for glass vials or containers molded from polystyrene, polyethylene, and the like. Low-density polyethylene is used for flexible plastic containers. High-density polyethylene, which is far more rigid, is generally used for a complete line of containers from small to very large capacity.

High-density polyethylene might be used in screw caps, but it must be studied for its stress cracking properties. The adherence of liners in polyethylene closures presents problems: a tacky or pressure-sensitive adhesive seems necessary due to the inert, wax-like surface of the polyethylene, which has excellent chemical durability that works against the common materials used for adhering liners in thermosetting molded closures.

Cellulose acetate and cellulose acetabutyrate have been used only to a minor extent in screw caps and snap-on caps, because of the high cost of raw materials. More recently, polypropylene, acrylonitrile, butadiene-styrene, polyamide (Nylon), polyoxymethylene (Delrin), and polycarbonate materials have become available. In time, with continued research, these materials will be improved and newer thermoplastic materials will be developed. These may lend themselves for use in closures when their cost declines.

Polyvinyl chloride and ethyl cellulose are also thermoplastic materials from which closures could be produced. However, their chemical nature or high cost makes them less likely to come into general use.

Molding Thermoplastic Closures

The various thermoplastic materials have different properties and their heat-distortion temperatures vary

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considerably. Some, such as the high-density polyethylene, may be steam-sterilized. Thermoplastics have different shrinkage characteristics, which require the designing of molds based on the rate and amount of shrinkage for each individual material. For example, a mold that will produce proper dimensions in polystyrene cannot be used for polyethylene or the other thermoplastics, because the finished cap would not have the desired T and E dimensions in the threads. For each thermoplastic the molding cycle, molding temperature, and molding pressures must be worked out. Experience in mold design, machine operation, and research is very important in the successful production of plastic caps.

After closures are molded experimentally from any of these materials, they must be subjected to laboratory test to determine their resistance to a particular product. Simple immersion tests or exposure to a product's vapors are inadequate. Closures must be tested under stress, since thermoplastic materials are frequently subject to stress cracking. I have seen several cases in which closures, although molded from a thermoplastic material with a cap supplied with a proper liner resistant to the product, failed in actual use, due to the action of the product, which remained on the threads in use. When a product is poured from a container, a drop or two may remain on the threads; then, when the cap is reapplied, the product has a chance to react on the cap, which is under stress, since it has been again tightly applied to the bottle. In these several instances, the cap side wall actually split after several days of use. Although the closure was not dissolved by the product, some of the materials used in the preparation penetrated the thermoplastic material, causing it to relax and permit cracking of the sidewall under the stress of application.

Many thermoplastic materials, although not dissolved by essential oils, are weakened by them. Generally, thermoplastic materials resist water, alcohol, and water-alcohol combinations. If essential oils or organic solvents, camphor, menthol, pine oil, or other such materials are present, however, some weakening may take place. I mention these properties to emphasize the need for careful laboratory studies. Whereas thermosetting molding materials are generally resistant to a wide variety of products including organic solvents, thermoplastic materials must be evaluated and checked as outlined above. The necessity of checking thermoplastic molded closures is similar to that for liner investigation in selecting a proper liner for molded or metal screw caps. There is a definite field for the thermoplastic materials in closures for some of their properties have advantages over those of thermosetting materials, especially with regard to torque strength and to dimensional stability under exposure to high humidities.

The industry has been interested in a linerless closure, but as yet, no entirely successful linerless

screw closure has been produced to fit rigid containers such as glass or those molded from high-density polyethylene.

Some years ago, a somewhat heavy-walled closure was molded from pigmented polyethylene and subjected to extensive field tests. In producing a closure of sufficient strength to prevent the cap from jumping the threads when applied to the bottle, insufficient accommodation was allowed in the top of the closure for the minor imperfections which are present even in good bottle finishes, and leakage resulted. For certain products a rigid molded closure without a liner can be used on a low-density polyethylene bottle finish, especially if the product is not highly volatile, for this polyethylene is resilient and flexible. However, extensive tests must be carried out.

On blown plastic bottles it has been found advisable to use a special type of thread known as the buttress thread, to give adequate strength. This requires molding a matching thread into the closure, to seal such a bottle finish. In other words, the present cap designed to fit standard GCMI glass finishes will not properly fit the buttress thread molded in the bottles.

To protect the valve on aerosol containers a cover is required. Such covers can be made from metal such as tinplate, or from one of the thermoplastic materials. Even for this use, careful laboratory studies are required to determine whether the product is compatible with the molded part.

Some thermoplastic materials are high in material cost, but have high strength characteristics as well as good chemical resistance. There is a natural tendency in making closures from such materials for commercial use to utilize less material, that is, to reduce the wall thickness. Frequently, under such conditions, the wall thickness will be too thin, and the cap will not be sufficiently rigid to function as a suitable closure when applied with sufficient force to seal the product. Therefore, a minimum wall thickness must be established for each material, in order to produce a functioning closure. If too much material is required, the cost is too high.

Advances will continue to be made in the closure field. Metal caps have been improved, thermosetting closures are now more versatile in design surface decoration and function, and thermoplastic closures offer a great variety of design and color possibilities, surface treatments, mechanical strength, and resistance to moisture; but they must be properly tested with the product actually being sealed for stress cracking.

As new packaging materials are developed, as bottles with higher fidelity and greater strength are produced, and as packaging lines are speeded up, there is a corresponding need for greater strength in closures. These needs will be met by research and engineering developments in the laboratories of closure suppliers. •

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(*Continued from page 783*)

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2,906,752—Norwich Pharmacal—1-(4-Chlorophenyl)-3-(5-Nitro-2-Furyl)-2-Propen-1-One.

2,906,753—W. R. Grace & Co.—Acyclic Hydrazinium Salts.

2,906,754—Monsanto—Unsymmetrical-1-4-Piperazines.

2,906,755—Schenley Industries—N-Acyl Derivatives of α Pyridine Carboxylic Acid Hydrazide.

2,906,757—Eli Lilly—Benzodioxanes.

2,906,758—Syntex—Hydroxyalkyl Ethers of Estradiol.

2,907,692—C. F. Boehringer (Germany)—Antidiabetic Composition and Method.

2,907,693—Chas. Pfizer — Antibacterial Compositions Comprising a Tetracycline-Type Antibiotic and A Quat. Ammonium Salt.

2,907,694—Chas. Pfizer—Halosteroids.

2,907,695—E. Adam etal.—Preparation Derived from Placental Tissue For Relieving Rheumatoid Arthritis.

2,907,697—Chas. Pfizer—Vit. B_{12} Composition.

2,907,758—G. D. Searle—Cyclo Epoxypregnanes.

2,907,759—G. D. Searle—Oxygenated Oxido Pregnen Diones.

2,907,760—J. R. Geigy—Bis Naphthylene Triazolyl Stilbenes.

FLAVORING ANTIBIOTIC PRODUCTS

(*Continued from page 749*)

not only from manufacturer to manufacturer, but also within each general flavor type. For instance, the simple term "cherry" is not descriptive, since there are many types of cherry flavor which are readily distinguishable from each other, that is, red cherry, black cherry, cherry pit, maraschino, cherry morello, sweet cherry, wild cherry, and burgandy cherry.

The flavor manufacturer attempts to produce as accurately as possible a true flavor type. These true types do not necessarily lend themselves to the unique "flavor solution" sought by the flavorist. A combination of such flavors will, when properly blended, yield a unique taste sensation, with no clashing of flavor notes.

Whenever possible, flavoring aids should be incorporated in the product to suggest a true "flavor profile." Thus, the use of fruit acids with citrus flavors provides the tart acidity expected by the consumer. A series of such acids are available to the formulator and small quantities of these acids will markedly enhance consumer acceptance. Some useful flavoring aids are listed below:

(1) artificial sweeteners—saccharine, cyclamates
(2) sodium chloride
(3) glutamic acid and monosodium glutamate[23, 24]
(4) fruit acids—citric acid, tartaric acid, malic acid
(5) Contra-Sweet—G. Lueders & Co.
(6) Palatone—Dow Chem.
(7) Cyclotene—Dow Chem.

The use levels of these additives vary from formulation to formulation, and the proper amount necessary must be predetermined. As a general rule, flavor levels for antibiotic syrups and suspensions will be in the range of 0.3 to 0.6 per cent for liquid flavors and 0.5 to 1.0 per cent for the spray dried flavors. It must be remembered, however, that taste differences may ensue with a change in the concentration of the flavor.

Spray dried flavors are especially useful in dry powder products for reconstitution and for tablets. Dry flavors also contribute to the stability of these products in that the active flavor components are coated and as a consequence cannot react with the medicament. The absence of moisture is also an advantage.

An ever-present problem facing the formulator is the possible reaction of the medicament with the components of the flavor combination. Since an individual flavor may consist of many reactive chemical compounds, degradation of the active ingredient by the flavor constituent may occur. Control studies must be run concurrently with the flavored samples to determine whether this effect is produced. Also of concern is the loss of flavoring agents due to aging. Many active ingredients will change with time, altering the character of the flavor. Accelerated temperature samples should be compared with refrigerated samples of the same formulation in a taste panel, in order to obtain a comparison evaluation.

When processing is done in open vessels, flavors can escape. Therefore, it is advisable to use closed systems. Stainless steel or glass-lined tanks should be used to prevent metallic contamination.

Control of *p*H is also of importance since a *p*H above 7.0 can cause hydrolysis of a great many of the flavor esters.

In some cases changing from citric acid to sodium citrate can result in a taste change, due to a change in *p*H. This is a factor to be considered if the stability of the product is satisfactory at a higher *p*H.

A major aid to the formulating chemist is the judicious use of a taste panel. The panel evaluation

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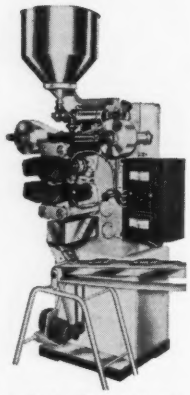

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method has been discussed by many authors.[25-29] At Pfizer we employ three types of panels, namely, the expert taste panel consisting of 10 to 20 individuals with a high taste sensitivity, the consumer taste panel consisting of a cross-section of company personnel, 40 to 50 people, and a children's taste panel consisting of approximately 25 children.

As a rule, the expert panel is used in the screening of the initial flavored formulas that the formulator deems acceptable. The panel rates a formulation on a numerical basis of one to nine. A rating of five or above is considered acceptable. A rating of nine indicates that it is liked very much, and a rating of one means it is disliked extremely. The numbers in between indicate varying degrees of like or dislike.

A mean rating is obtained by multiplying the key numbers by the number of panelists indicating this choice. The sums of these products are then divided by the total number of panelists.

A typical expert taste panel report is shown below.

Product: Urobiotic for oral suspension
A. (peach-custard)
B. (cherry-vanilla)
Object: Taste comparison and evaluation
Method: Paired comparison
Results: Cherry-vanilla is the preferred flavor combination
Mean ratings: A. (peach-custard) 4.73
B. (cherry-vanilla) 6.67

Distribution of Judgments

Key	Number	A	B
9	Like extremely	–	1
8	Like very much	–	3
7	Like moderately	3	4
6	Like slightly	3	5
5	Neither like nor dislike	2	1
4	Dislike slightly	2	1
3	Dislike moderately	4	–
2	Dislike very much	1	–
1	Dislike extremely	–	–
	Total judgments	15	15
	Mean rating	4.73	6.67

The report can also be expressed in the following way:

	A	B
Favorable	6	13
Neutral	2	1
Unfavorable	7	1
Total	15	15

Comments: Pleasant taste in cherry-vanilla samples, but flavors seem a little weak. Slight bitter, medicinal aftertaste in both. Color pleasant in both samples.

The major problem of flavoring antibiotics is the characteristic bitterness associated with this class of drugs. There are no adequate terms to describe the individual degrees and types of bitterness that one encounters. The bitterness obtained from nystatin differs from that of tetracycline or triacetyloleandomycin. Each antibiotic formulation presents a separate problem and must be handled as such.

There are approaches other than that of actually trying to mask the bitterness, such as the preparation of insoluble salts and the coating of the active in-

gredient. The availability of the drug for absorption should be uppermost in the formulator's mind. The use of ingredients that impair proper utilization and absorption should be avoided. An example of the formation of a more insoluble tasteless form is calcium dioxytetracycline, soluble 0.030 mg./ml., as compared to oxytetracycline, soluble to the extent of 0.5 mg./ml. at *p*H 5.0.[30]

The use of erythromycin ethyl succinate is claimed to eliminate the bitter taste associated with erythromycin products by virtue of its insolubility. Palatable aqueous suspensions of chloramphenicol can be made by the use of the palmitate ester.

Oral liquid formulations of antibiotics are dispensed in the following forms: suspensions in oil (corn, coconut and peanut oils), aqueous suspensions, and solutions.

Each type of product requires separate consideration in the choice of a flavor. It has been our experience, when using oils as vehicles, that coconut oil appears to be less "oily" in taste. Custard, butter-caramel, butterscotch, caramel and coconut-custard flavors give a satisfactory base flavor. To one or a combination of these a "top note" may be superimposed which will give a smooth flavor to match both the chosen color and the oily taste of the vehicle.

By far the largest group of oral liquid antibiotic preparations are the aqueous suspension group. These may either be "ready mixed," suspensions utilizing combinations of water, sorbitol and sugar syrups, or suspensions for reconstitution. Antibiotics included in this class are the tetracycline group, nystatin, triacetyloleandomycin, erythromycin esters, chloramphenicol esters, novobiocin, and penicillin derivatives such as benzathine penicillin G and phenoxymethylpenicillin.

Suspensions of this type are by necessity sweet. However, depending upon the nature of the drug in suspension, additional artificial sweeteners usually are required. In this group the greatest individuality may be expressed and the art and science of the antibiotic flavorist reaches its peak. While not intended to be "beverage perfect," acceptance by children is a necessary condition for a good antibiotic suspension. Some 70 to 75 per cent of antibiotic suspensions are fruit flavored.

The specific recommendations for the various types of antibiotics, based on our experience and observations, are as follows:

Tetracycline Group. This group includes oxytetracycline, which is used as the amphoteric base or calcium di-oxytetracycline, tetracycline used as the amphoteric base, or its calcium or magnesium chelate and chlortetracycline used as the calcium chelate. These chelates are extremely insoluble and as a result a more palatable product can be produced.

The tetracycline drugs lend themselves admirably to cherry, raspberry, and citrus flavors.

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TABLE 1

Color and Flavor Preference of Foreign Nations—Pharmaceuticals

Country	Acceptable colors	Objectionable colors	Acceptable flavors (liquid)	Objectionable flavors (liquid)
Brazil	yellow red orange pink white	brown black	raspberry cherry orange tangerine vanilla	chocolate lemon banana peppermint caramel
Greece	light green yellow white red light red	black blue	chocolate banana strawberry raspberry apricot	lemon mint cinnamon
Portugal	red yellow green blue	black white gray brown	strawberry orange banana lemon raspberry	licorice peppermint sarsaparilla anise vanilla
Spain	white light green light blue yellow red	black violet brown gray dark colors	strawberry lemon orange mint vanilla	wild cherry anise cinnamon cocoa almond
Australia	white orange yellow red green	violet black brown blue gray	raspberry strawberry lemon cherry vanilla	spearmint wintergreen almond anise
Japan	white* light red* light orange*	yellow* salmon red dark colors	raspberry vanilla	"sweeter than actual flavors"
Puerto Rico	red yellow green pink orange	black brown blue gray white	raspberry orange cherry banana peach	chocolate peppermint anise vanilla lemon
Austria	red orange yellow coffee white	green blue violet dark brown black	chocolate banana raspberry cherry peppermint	menthol currant

*Liquids Only

Penicillin Group. The penicillins are usually dispensed as insoluble salts such as benzathine penicillin G and penicillin V, which is used as the benzathine or hydrabamine salt. These salts utilize the milder flavors of banana, peach, vanilla, coconut, custard, fruit, and various combinations of the aforementioned to provide a unique flavor solution for each company marketing the product.

A soluble derivative, potassimu penicillin G, is used in troches and in products for reconstitution. These products may be flavored with either cherry or citrus, and perhaps some mint. A stronger level is required due to the solubility of this salt. This is also true in the case of the soluble salt, potassium penicillin V.

Macrolide Group. This includes TAO (triacetyloleandomycin), which shows a marked decrease in solubility over a oleandomycin base. This lends itself to the formulation of a palatable aqueous suspension. Fruit flavors such as cherry, raspberry, strawberry, blended with custard, apple, or apricot, give satisfactory results.

Erythromycin as the ethylsuccinate, ethylcarbonate and stearate esters are satisfactorily flavored with members of the citrus group.

Polyene Group. Nystatin has an exceedingly low solubility in water; despite this, it is extremely bitter tasting and requires a strong citrus or cherry flavor to mask fully the lingering bitterness of this drug. It is usually sold in combination with tetracycline.

Soluble antibiotics such as dihydrostreptomycin sulfate and neomycin sulfate lend themselves to citrus and peach flavors. These antibiotics are not as bitter or as harsh in taste as the other types, and are not too difficult to flavor.

Miscellaneous. The bitter taste of chloramphenicol made the preparation of liquid products very difficult. This was overcome by the synthesis of chloramphenicol palmitate, which may be satisfactorily flavored with custard.

Novobiocin as the calcium salt is available for use in liquid preparations and can be flavored with citrus or fruit, in addition to a mild flavor such as custard for fuller body.

Bacitracin or zinc bacitracin, polymyxin B sulfate, tyrothricin, and gramicidin are commonly used in troches. They require a high flavor level to insure a pleasant taste until the troche has completely dissolved. Fruit flavors, such as cherry, citrus, and mint types, are most commonly used. When compounding

the "hard candy" type of troche, care must be used in selecting a flavor that can stand some degree of heat, since elevated temperatures are used in the manufacturing process.

To summarize, the flavoring of antibiotics is still mainly empirical. We have presented an approach to this problem which may be used as a guide. The evaluation method, by which a choice may be made between flavor combinations, has been found to be a most feasible and satisfactory one.

We believe, finally, that an analogy can be drawn between the art of the perfumer and that of the flavorist. The perfumer must remember the odors of hundreds of scents, and the flavorist should have the same type of memory and be able to recall a like number of flavors. He should then be able to utilize this "flavor memory" in the preparation of his dosage form.

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METHIONINE

(*Continued from page 761*)

strength and sulfur retention in the granulation tissue. Histologic research on the effect of methionine in wound healing was made by Perez-Tamayo.[17] Research at Harvard Medical School[18] has shown that methionine can exert a positive influence in improving the efficiency of protein metabolism from body tissues and thus allow a more extensive utilization of nitrogen in repairing wound tissue. The Harvard workers postulated that methionine restores the accumulation of mucopolysaccharides and the forma-

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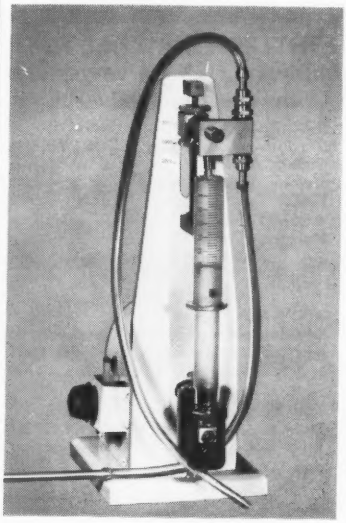

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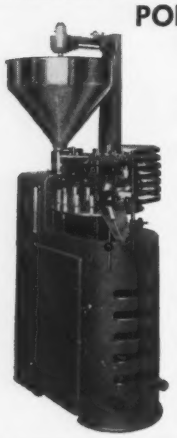

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tion of collagen fibres to levels which approximate the normal.

Allantoin and its various derivatives[19, 20] have been found useful for external application in cosmetic and pharmaceutical preparations because of epithelizing properties stimulating formation of normal cell tissue. Stable compounds of allantoin and its aluminum salts have been made from methionine and its derivatives. It appears that they may become useful adjuvants in cosmetic and dermatological therapy.

Absorption through Skin. British investigators[21] have provided some interesting data on the rate and extent of absorption of methionine through the skin using radioactive tracer studies. This means that some of the interesting polyfunctional properties of methionine can be utilized by formulators of cosmetics, toiletries, and topically applied medications. It was found that absorption by the skin had nearly half the efficiency of oral feeding as measured by the radioactivity of hair clippings of test animals. Commercial preparations containing DL-methionine along with other ingredients for topical use are presently appearing in this country and overseas markets. Aerosol sprays are also being explored.

The effectiveness of methionine as an active agent in a therapeutic compress has been evaluated by Lubowe[22] and Pomeranze. A stable, nonodorous colloidal complex was formulated which had advantages over the usual antiseptic solutions such as aluminum acetate, potassium permanganate, or silver nitrate. Clinical trials with this moist antiphlogistic compress have demonstrated its effectiveness in the early treatment of infectious and eczematous dermatitis. No incidence of sensitization has been observed in the treatment of a large number of clinical cases. The compress does not stain and can be helpful in removing the crusts which appear in pyogenic dermatitis. Varicose and decubitus ulcerations seem to heal rapidly with this treatment. It acts as an epithelial stimulant and assists in clearing up the crusts which appear on the face after dermabrasion. It should be mentioned that an outstanding feature of DL-methionine and its derivatives is its relative epidermal safety.

Ulcer Treatment. Turner[23] provided 3-6 grams of DL-methionine in divided doses to a group of chronic peptic ulcer patients who were given the amino acid preoperatively only to see if a favorable effect could be obtained on the healing of ulcers prior to surgery. Another group was given methionine for the purpose of long-term therapy of patients with duodenal and gastric ulcers. Fifty-four cases with chronic peptic ulcer have been treated over a period of four and a half years with good clinical results in 80 per cent of the patients. These findings suggest that there may be a relationship between sulfur amino acid metabolism

and the pathogenesis of peptic ulceration. Turner refers to earlier observations in the field of protein metabolism and wound healing by previous investigators. It was pointed out that a typical chronic peptic ulcer patient could undergo some kind of stress which results in metabolizing and excreting excessive amounts of sulfur-containing substances such as gastric mucin. This loss could very well result in a partial deficiency of essential amino acids, and diminish the resistance of the gastroduodenal mucosa to autodigestion.

Dermatological Therapy. The oral use of methionine has been described for verrucae (warts) by several clinicians[24-26] as beneficial and leading to their eventual disappearance. Favorable results in using methionine for the more painful plantar varieties have also been reported.[27] Resistant cases of condylomata acuminata have been treated successfully with oral methionine.[28] It has been observed in clinical dermatological practice that the combination of methionine with an antibiotic, such as tetracycline, seems to be more effective when used simultaneously for the treatment of verruca plana, particularly of the face.

Messerklinger[29] described the treatment of laryngeal papilloma with oral doses of methionine. Surgery and electro-dessication were not found effective. There was oral treatment of the recurrent growing papilloma following surgery with 0.5 gram of methionine given three times daily. The papilloma disappeared and did not return. The results were most unusual. Methionine therapy was simpler than surgery. Further studies in this field are warranted.

Methionine and Nitrogen Metabolism. Diaper dermatitis of infants occurs with great frequency in the United States and has been a disturbing clinical entity to both the parent and child. Several methods are presently used involving topical or internal therapeutical agents. Silicones, allantoin lotions, corticosteroids, quaternary compounds and antibiotics, such as neomycin, can be used topically in various combinations. Goldstein[30] demonstrated the value of using methionine additions to infant oral formulas for the treatment and prophylaxis of diaper dermatitis. All but three of the 500 infants studied showed a disappearance of the ammoniacal odor from the urine in three to five days. It was also found that using methionine brought about optimum weight gains of the infants. The work of Goldstein and his success in decreasing excretion of urinary nitrogen encouraged Bergman[31] to try adding methionine to the diet of patients in a mental hospital. Control of the odor from ammoniacal urine has been a chronic problem in the management of institutions where incontinence and enuresis occur with great frequency. Many remedies for controlling the odor had been suggested and tried; however, they were

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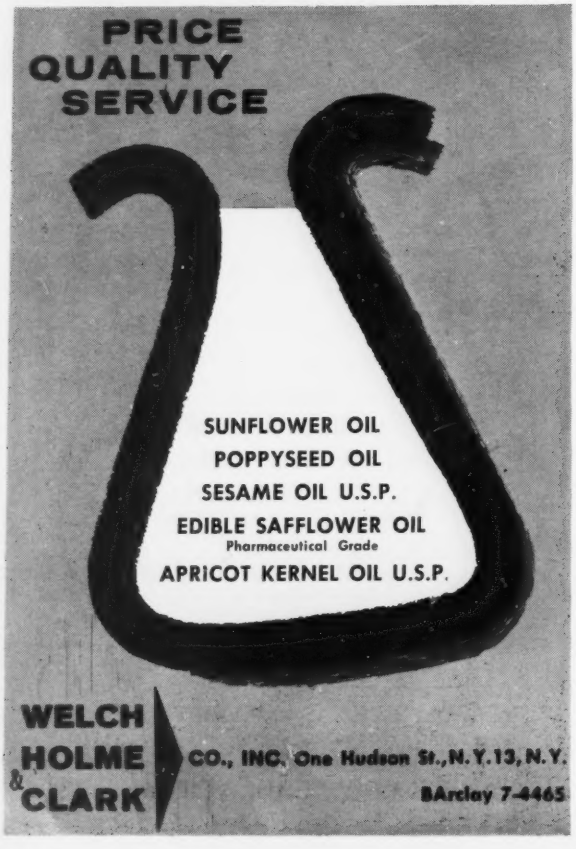

discarded because they were either ineffective or too expensive. Bergman tried doses of 0.2 gram of methionine in capsule form provided three times daily. Two groups of patients were studied, one consisting of 16 bedridden females with spastic paralysis and the other a group of 70 males, mostly youngsters. All were incontinent to the point of constant saturation. One-half had dermatitis and several had skin inflammation and ulceration. Three capsules a day controlled the odor. However, in cases of severe skin involvement, it was necessary to increase the daily amount to four capsules. As a control measure, methionine capsules were withheld and, within three days, the offensive odor returned, along with the dermatitis in cases where it had existed previously. Upon reinstitution of treatment, odor and rash disappeared.

Rosenberg[32] prescribed a dose of 0.2 gram of methionine three times daily to control incontinence and urinary odor in ten patients ranging in age from 74 to 88 years. There was a marked reduction in urinary odors and genital dermatitis. With increased emphasis these days for the care of the aged, not only in mental institutions but also in nursing homes, methionine can help considerably to minimize these problems.

Urinary Tract Infections. The acidification of urine on high intake of methionine for the treatment of urinary infection has been described by Kass.[33] In working with patients having stubborn urinary tract infections completely resistant to antibiotic therapy, Kass found that high-level ingestion of methionine not only reduced the *p*H but also the bacterial count of the urine. He postulated that some unknown metabolite is formed from methionine in the body which has a bactericidal effect on the resistant organisms.

High-level consumption of methionine carries with it a note of caution. Iowa medical researchers[34] studied prolonged feeding of 8 to 12 grams of DL-methionine daily to humans, in addition to a normal diet carrying about 4 grams daily. There were lowered levels of prothrombin and accelerator globin. This same mechanism has been observed by feeding cysteine. By adding glycine and arginine to a DL-methionine supplement, the toxicity of the excess sulfur amino acid can be reduced or eliminated.[35] One must note in this case that the synthesis of tissue protein becomes enhanced.

Pomeranze and Lubowe[36] have prepared stable reaction products from various organic acids and methionine derivatives which show promise for starting a new series of non-toxic wide-spectrum urinary antiseptics. Early clinical studies appear promising.

Metabolism in Mental Diseases. Recently the biochemical and medical professions have become greatly interested in preliminary psychiatric and neuro-

therapeutic findings just reaching this country from Russian investigators.[37] Following up previous literature that methionine helps regulate liver metabolism, the researchers carried out experiments with methionine for the treatment of schizophrenia in a psychiatric clinic. In order to explain some of the mechanisms involving the therapeutic action of methionine, complete blood and urine studies were made and correlated with plethysmographic and pneumographic findings. Patients were examined before, during and after treatment. Biochemical findings pointed up a return to normal of the ammonia index of patients' urine. Blood findings also demonstrated normalization of ammonia and glutamine values after being on a methionine program. It is of interest to note that all kinds of modern treatments had been given previously to these patients for many years without any results. With methionine treatment, normalization of vascular reflexes preceded clinical improvement. The Russian workers felt that methionine provokes direct metabolic changes on the cells of the liver. American workers have already started to explore the possibilities of using methionine by itself, as well as in combination with recognized tranquilizers for the treatment of mental diseases. Of interest in this connection is the report on DL-acetyl-methionyl-N^2-isopropyl hydrazide (Ro 4-1018) as a new drug to combat emotional depression.[38] The approach of using amino acids as aids to alter metabolic pathways influencing psychological reactions and stress conditions will undoubtedly receive great attention in the next few years.

Role in Atherosclerosis. Much has been written on the role of methionine in reducing atherosclerosis in experimental animals[39, 41, 46] and humans.[42] Stammler's work at the Michael Reese Hospital in Chicago[43] has shown that an inadequate methionine intake led to increased hypercholesterolemia, coronary and aorta atherosclerosis in chicks on cholesterol-oil-rations. Labecki[44] and Morrison[45] have shown the favorable effects of methionine as part of a lipotropic mixture for restoring to normal the serum cholesterol-phospholipid ratios in coronary artery disease of humans. Russian work[46] with methionine, pyridoxine and ethyl esters of linoleic and linolenic acids also mentions lowered blood cholesterol levels in patients receiving mixtures of all three types of compounds for a period of 20 days.

Radiation Injury. The rapid pace of technological achievement will thrust man's bold ventures into space quite soon. Evaluation of biological requirements under stress conditions to find out what it takes for man's survival in space for a few hours or a few months will be a great challenge to our scientists. Future space exploration will necessitate greater studies on compounds like methionine whose polyfunctional properties can protect biological systems

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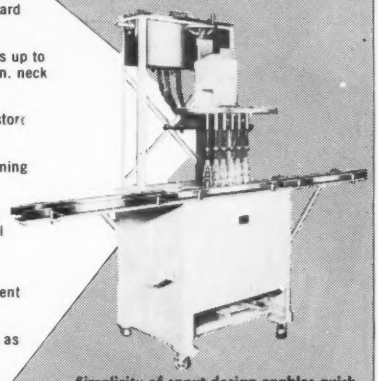

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Examination of the metabolic pathways of organic sulfur compounds has a great future, since these compounds offer great potentialities as protective agents against the hazards of ionizing radiation and other types of rays which interfere with formation of nucleic acids. Methionine, which contains an active S-methyl group, is quite radiolabile and can be destroyed by *in vivo* and *in vitro* experiments after exposure to ionizing types of radiation.[47] Workers at the Indian Cancer Research Centre in Bombay[48] have found that post-irradiation administration of methionine is more effective in arresting the fall in nucleic acid levels caused by exposure to radiation than pre-irradiation treatments. Replacement of methionine helps keep the nucleic acid synthesizing mechanism in order and is responsible for the favorable therapeutic influence on radiation injury. This area of research has much in store for the cosmetic and pharmaceutical industries.

Summary

Methionine occupies a significant place among essential amino acids because of its important polyfunctional properties, in addition to the role as a structural unit of body proteins. The commercial synthesis of DL-methionine has accelerated new formulations of this sulfur amino acid in cosmetics, dermatologicals, and pharmaceuticals.

Radioactive tracer studies have demonstrated that its absorption through the skin suggests greater usefulness of topical approaches for therapy. An outstanding feature of this amino acid is its relative epidermal safety.

Since clinical and laboratory findings indicate improved nitrogen metabolism following intake of methionine, its usefulness in the treatment of peptic ulcer and disturbed emotional behavior has been established. Since methionine aids in restoration of normal serum-cholesterol phospholipid ratios in atherosclerotic diseases, it merits greater attention by researchers in this field.

Space age problems will demand additional research on the potentialities of methionine as a protective agent to reduce the hazards of ionizing radiation.

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PHARMACEUTICAL ADVERTISING

(*Continued from page 753*)

allowed to go? If a calculated risk means that we expound untruthfulness in order to sell—that is, abrogate our first principle of pharmaceutical advertising in order to enhance the second—then, I think the question answers itself. We are charged with a public duty and there can be no excuse for any form of misrepresentation of our products or their therapeutic capabilities. The only risk that conceivably might be taken in pharmaceutical advertising would be to present the truth in a novel, unique, or yet untested fashion.

And now, what is the role of the lawyer—both ideally and as a practical matter—in this challenging field of pharmaceutical advertising? It seems to me that the lawyer practicing in this unique area of the law can and should be a several-fold personality, having the ability to work unobtrusively with the people who create, and objectively with the laws and regulations that must be administered, and also having the necessary principles to insist upon reasonable compliance with applicable regulations but with a firmly constructive attitude in their interpretation and application. I enjoy the stimulation of the advertising fraternity; I respect the creative talents of the advertising people with whom I am privileged to come in contact; I respect the freedom they require in order to operate effectively. But, even though recognizing these considerable values, I have never been convinced that a certain amount of discipline smothers creation. Nor, on the other hand, am I con-

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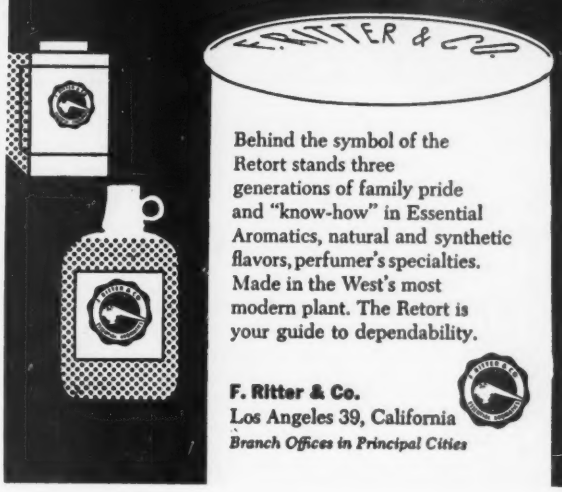

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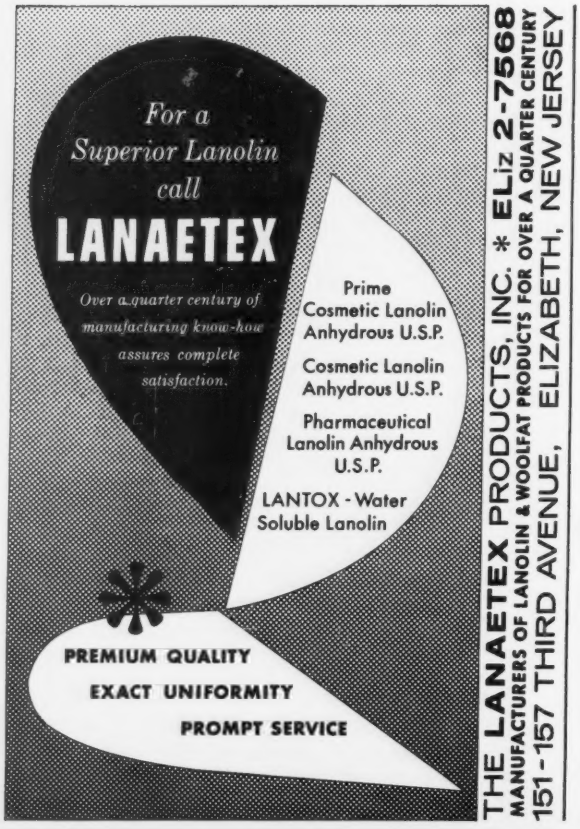
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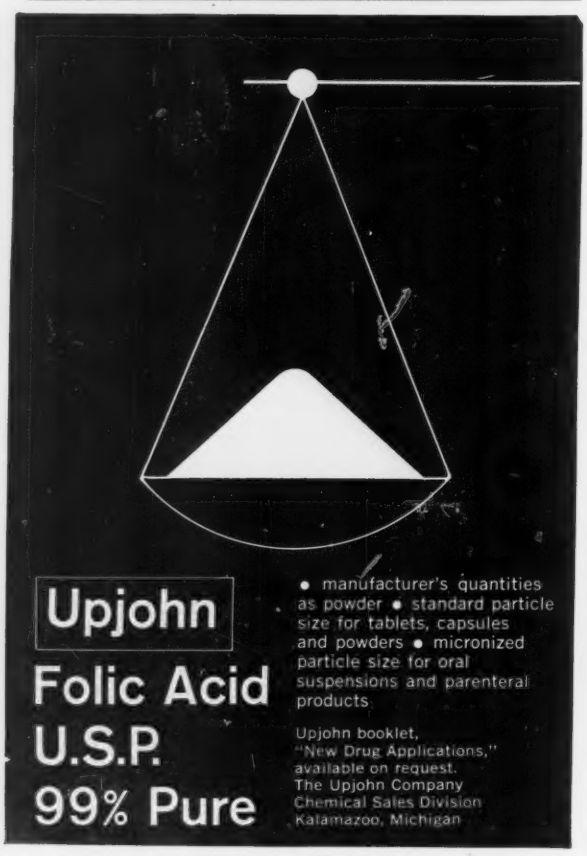
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vinced that an overabundance of regulation leads to an effective or attractive system. It is my belief that the greatest contribution the legal profession can make in this field is to take the burden of worry from the deliberations of the creative people within our organizations. Ideally, our contribution should allow for the unhindered use of such talent in the sale and promotion of the products of the company without concern for anything but truth and good taste. And then it should become the function of the industry attorney to temper the exuberant flair of creativity with the enlightened conservatism of his profession. No lawyer in this field should attempt to step into the arena of creativity, and thus hamper advertising's prime function, but he should be invited to lend his practical knowledge of the law and the industry to provide proper guidance through the maze of regulation surrounding advertising's efforts.

I do not recommend that we give up the hard sell. In the fierce climate of competition in our industry, we cannot let our guard down for a moment. We must continue to promote our products, but we must also insist that such promotion never become suspect. I am convinced that we will come out of this period of heavy investigation of our industry and prove that we can handle ourselves without the interference of further government regulation. If we do not prove that we are thus competent, then we deserve the censure of the public and the regulation of the government.

What of the future? What can we do together to insure our continued success? Here are a few suggestions:

(1) We should recognize that at this time in the growth of pharmaceutical manufacturing we are faced with a problem greater in scope than the problems of any one of our single clients, and in this connection we should pay increasing attention to institutional advertising calculated to sell our industry. Manufacturers will be faced with increasing attempts to cast doubt upon their motives and operations. Advertising holds the all-important key to public opinion.

(2) We should continue to provide the health team with full and proper information regarding the products we sell.

(3) We should continue to provide the public with full and proper information about the products which we, under the law, may sell directly to them.

(4) Our advertising people and our lawyers should continue to exchange constructive views and criticism for the purpose of accomplishing that which is, after all, our common goal—the increased sale of our companies' products—without question as to the good faith of our efforts.

(5) Finally, we should be vocal at every opportunity in our insistence upon our right to regulate ourselves, and our activities should reflect our ability to do so. •

Industry's Books . . .

Soil, Grass and Cancer (health of animals and men is linked to the mineral balance of the soil) *by Andre Voisin, Member de l'Academie de'Agriculture de France, Translated from the French by Catherine T. M. Herriot and Dr. Henry Kennedy, 302 pp., Philosophical Library Inc., New York (1959), cloth,* **$15.**

"There is a great deal of interest at the present time in trace elements and the nutrition of man and lower animals, interest which has, of course, been enormously stimulated by the discovery of the tremendous importance of traces of cobalt, copper, molybdenum and other elements in the soil. Sir Albert Howard, Sir Robert McCarrison and others have stressed the possibility of such deficiencies occurring in our diets as we process and sophisticate foods increasingly and particularly through the use of chemical fertilizers in agriculture. The author puts together a great deal of recent information in his work which is well documented and provocative." The above is quoted from H. M. Sinclair D.M., B.Sc., University of Oxford.

Disease Detectives (Your Career in Medical Research) *by Harry Edward Neal, 192 pp., Illus., Julian Messner, Inc., New York (1959), cloth,* **$3.50.**

Here are behind-the-scenes glimpses of real scientists at work in modern medical research laboratories. First-hand accounts from on-the-spot observations and personal interviews show not only some of the marvelous achievements of medical science, but also some of the perplexing problems that remain unsolved, offering a dramatic challenge to the new generation of science explorers still in high school and college. Of interest to the general reader.

Current Drug Handbook—1959-60, *by Mary W. Falconer, R.N., M.A., and H. Robert Patterson, B.S., M.S., O'Connor Hospital, San Jose, Calif., 160 pp., W. B. Saunders Co., (1959), paper bound,* **$2.75.**

This book contains specific, technical data on approximately 1000 drugs in current use. It is intended for quick reference and to supplement the material in standard textbooks of pharmacology, specifically, Falconer-Norman: The Drug, The Nurse, The Patient.

May's Chemistry of Synthetic Drugs, Fifth Ed., *Revised and Rewritten by G. Malcolm Dyson in Consultation with Percy May, Size 9¼ x 6⅛, Longmans Green & Co., New York (1959), cloth* **$22.50.**

The fifth edition of this work has entailed complete rewriting of all sections. The enormous growth of the subject since the publication of the fourth edition in 1939 has made unworkable the subdivision into chapters according to chemical classification. The author has, therefore, redistributed the material according to the biological activity of the drugs, except for a part of the field of chemotherapy in which the retention of special sections devoted to the consideration of dyestuffs, sulphonamides, the organo-metallic compounds, and antibiotics assists in clarifying the subject matter. This work should be of special interest to research chemists, chemical laboratories, university departments of chemistry and biochemistry, and libraries in universities and the large chemical firms.

Diseases of Medical Progress, *by Robert H. Moser, B.S., M.D., Major, Medical Corps, U. S. Army, 131 pp., Charles C. Thomas, Publisher, Springfield, Ill. (1959), cloth* **$4.75.**

Illness, induced by well-conceived therapy, emerging as the patient is being treated for the original process, is a traditional nemesis well-known to the practicing physician. This work covers: hormone-induced diseases; antibiotics-induced diseases; pulmonary diseases; collagen and collagen-like diseases; renal diseases; cardiac diseases; metabolic diseases; dermatologic diseases; hematologic disease; neurologic disorders; hepatic and gastrointestinal diseases; psychiatric diseases; diagnostic and therapeutic radiation-induced diseases; and surgically-induced diseases.

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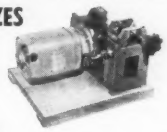

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